Seeing emotion: Studies on the processing of facial expressions in normal development and young children with autism

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1 General introduction

Chapter 1

1. General Introduction

Rapidly perceiving the emotional content of a face is an important skill for successful social behavior, since it helps to evaluate the states and intentions of others and to adapt future behavior accordingly. One of the ways in which the visual system captures environmental information, like facial expressions, is in terms of luminance variations that vary across space. High spatial frequencies (HSF) represent abrupt, small luminance changes, corresponding to sharp edges and fine perceptual detail. Low spatial frequencies (LSF), on the other hand, represent global changes in luminance, and provide information about the general shape, proportions and large contours of objects in our visual environment (Bar, 2004; Goffaux & Rossion, 2006; Morrison & Schyns, 2001). Several studies in adults have indicated that particularly LSF information plays an important role in the rapid processing of facial expressions (e.g. Pourtois, Dan, Grandjean, Sander, & Veuilleumier, 2005; Holmes, Green, & Vuilleumier, 2005).

This perceptual side of facial expression processing is often overlooked, and is hardly taken in consideration when studying the development of normal and abnormal processing of facial expressions. Any abnormalities in low level visual perception early in life could lead to difficulties with processing emotional expressions from faces. As a consequence, this might lead to abnormalities in social interaction, considering that facial expression processing forms an important basis for communication and social development early in life when language is relatively immature. Indeed, basic visual processing deficits have recently been suggested to underlie the face processing difficulties that have been found in children with Autism Spectrum Disorder (ASD), (Johnson, 2005; Behrmann, Thomas, & Humphreys, 2006).

The experiments described in this thesis, among others, address whether there are developmental differences in the type of spatial frequency information that is important for facial expression processing across childhood. In addition, the experiments examine whether abnormalities in spatial frequency processing are present in young children with Autism Spectrum Disorder (ASD) and whether this is related to abnormal facial expression processing in this group.

In this introductory chapter, first some general background information and explanation of concepts will be given to introduce the research questions that are covered in this thesis. First, the concept of spatial frequencies will be explained. Thereafter, a review will be given of studies that have investigated the role of spatial frequencies in facial expression processing in healthy adults, followed by a discussion on the development of this relation in childhood. Subsequently, a short review will be given of the current knowledge pertaining to visual perception (especially spatial frequency) deficits in ASD. At the end of this chapter the general research aims and additional questions are outlined.

1.1 Spatial frequency processing: a fundamental aspect of vision

Our visual environment is complex and contains a lot of information: orientation, areas of light and dark at particular locations etc. The visual system captures this environmental information in terms of luminance variations (e.g. Goldstein, 1999; de Valois & de Valois, 1988). Luminance variations occur in a wide range of so called 'spatial frequencies' which can be expressed in cycles per degree (c/d) of visual angle. Figure 1 presents two grating patterns differing in spatial frequency (SF) content. The grating pattern at the left has a lower variation (0.5 c/d), and thus has a lower SF compared to the grating pattern at the right.

High spatial frequencies represent abrupt, small luminance changes, corresponding to sharp edges and fine perceptual detail, like for example the wrinkles in a face or stripes on a shirt. Low spatial frequencies on the other hand represent global changes in luminance and provide information about the general shape, proportions and large contours of objects in our visual environment (Bar, 2004; Goffaux & Rossion, 2006; Morrison & Schyns, 2001).

Direct evidence that HSF and LSF are respectively involved in local and global processing of stimuli, comes from studies investigating the processing of compound stimuli. Compound stimuli are stimuli that consist of a large shape which is built up of smaller shapes of either the same or different identity (for example the letter H built up out of X's; the global level is the letter H and the local level the X's). Participants have to identify targets at either a local (level of the smaller shape) or global level (level of the larger shape). Several studies have shown that processing at the local level is primarily mediated by HSF whereas global processing is driven by LSF (Boeschoten, Kemner, Kenemans, & Engeland, 2005; Shulman, Sullivan, Gish, & Sakoda, 1986). Besides its involvement in local and global processing, the differential processing of HSF and LSF by the visual system plays a central role in several other basic perceptual phenomena including natural scene recognition (Peyrin, Baciu, Segebarth, & Marendaza, 2004), motion perception (see for review Hess, 2004) and face processing (see for review Ruiz-Soler & Beltran, 2005; Goffaux & Rossion, 2006).

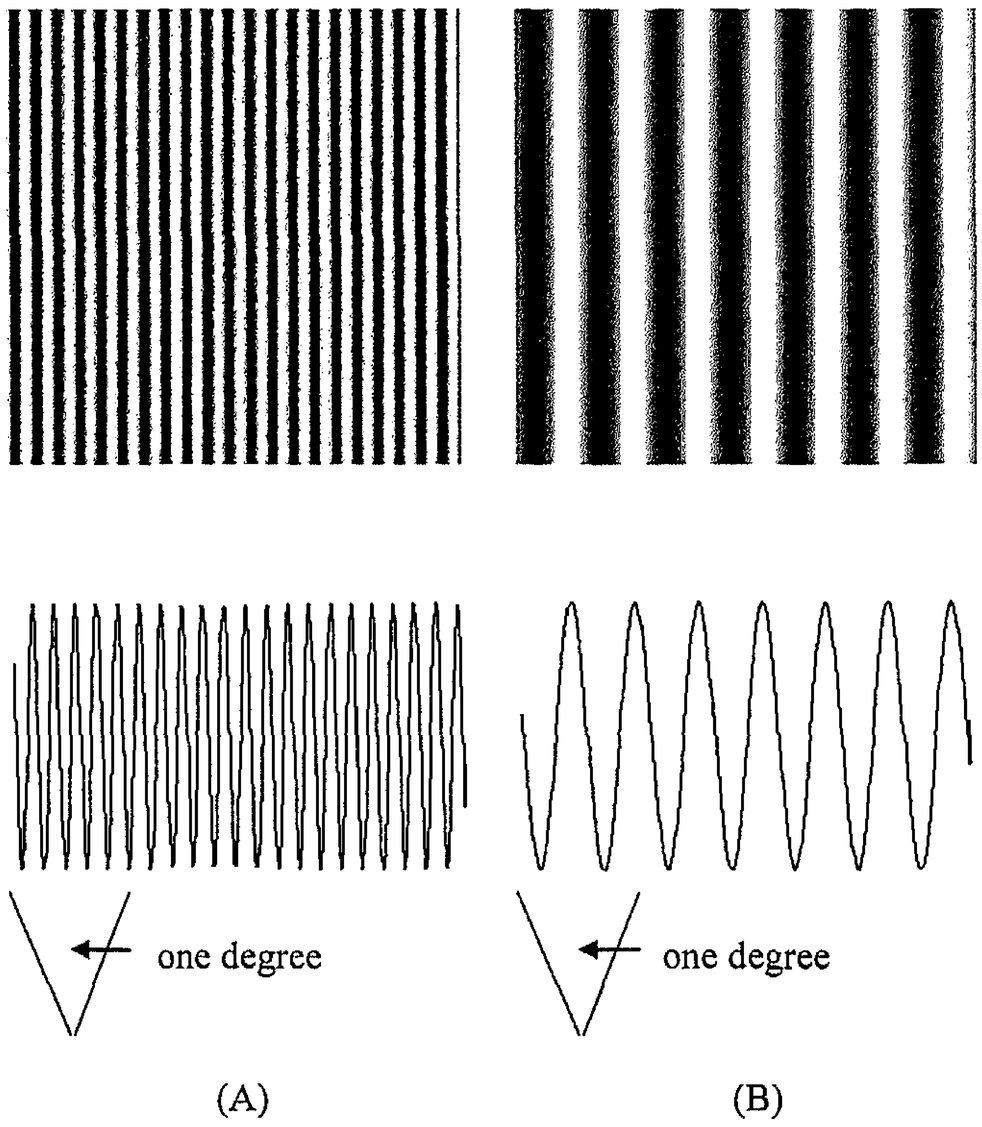

Figure 1. depicts two grating patterns (upper) and their corresponding frequency function (lower). The spatial frequency content of a stimulus is generally expressed in number of cycles per degree of visual angle. The grating at the left (a) has a higher number of cycles per degree (higher SF) compared to the grating at the right (b).

Important for the experiments described in this thesis, there are several indications that HSF and LSF information are processed differently by the visual system. Studies focusing on neuronal activity in the Lateral Geniculate Nucleus (LGN), the first relay point after the retina, indicate that two cell types in the LGN respond differently to HSF and LSF: parvocellular (small receptive fields) and magnocellular neurons (large receptive fields). Several studies have indicated that although parvocellular and magnocellular neurons respond to an overlapping range of SFs, parvocellular neurons are preferentially tuned (most active) to HSF, whereas magnocellular neurons are more sensitive to LSF information (Derrington & Lennie, 1984). Parvocellular and magnocellular cells project to cells in different layers in the primary visual cortex (V1), which continue to show different SF preferences (Tootell, Silverman, Hamilton, Switkes, & De Valois, 1988). Because the conduction velocity of axons of the parvocellular system is lower compared to the magnocellular system (see Hess, 2005), the response latencies of magnocellular neurons in the input layers of the primary visual cortex (V1) are 10-20 ms faster than those of parvocellular neurons

(Schmolesky et al., 1998). But note that other researchers suggest a smaller difference (see for review (Skottun & Skoyles, 2007)).

Also at higher levels of the visual system there are indications for differential processing of HSF and LSF. This evidence comes from fMRI and Event Related brain Potential studies (ERP), which are well suited to investigate neuronal differences in SF processing at a more macroscopic level reflecting activity in whole populations of neurons. These studies indicate that whereas LSF's elicit relatively strong activations in secondary (more higher order) visual areas, HSF's seem to predominantly activate more primary visual areas. Some authors have related this to the more extended and direct innervation of secondary areas by the magnocellular pathway (see for review Kenemans, Baas, Mangun, Lijffijt, & Verbaten, 2000). Others have related this difference in activity to SF between primary and secondary areas, to an increase in receptive field size from primary to secondary visual areas (see for review Henriksson, Nurminen, Hyvärinen, & Vanni, 2008).

In sum, there are several lines of evidence that indicate that HSF and LSF information serve different visual functions: respectively detailed and global processing. Also there is evidence that HSF and LSF information is processed differently at several levels of the visual system. First, there are indications that LSF information is processed faster compared to HSF information. Second, although there is some overlap, there is evidence for differences in SF selectivity in different cell types and brain areas. Important for the experiments in this thesis, these fundamental differences in SF processing, e.g. timing as well as location, can be measured with ERPs.

1.2 Spatial frequencies and facial expressions

Most relevant for the studies presented in this thesis, there is evidence for a differential role of HSF and LSF in facial expression processing. Two fMRI studies have now provided evidence for the importance of particularly LSF information in emotional expression processing. One study showed that LSF information in a face is crucial to produce an increase in activation to fearful relative to neutral faces in the amygdala (Veuilleumier, Armony, Driver & Dolan, 2003). The amygdala is considered to be a key structure in emotional processing, as it initiates rapid motor and autonomic responses to emotional events (Morris, Ohman & Dolan, 1999; Whalen, Rauch, Etcoff, McInerney, Lee & Jenike, 1998). In contrast, Veuilleumier et al. (2003) showed that high spatial-frequency (HSF) information in faces did not evoke a differential response to fearful compared to neutral expressions in the amygdala. A similar pattern of results was found in the fusiform cortex, an area specifically associated with the processing of faces (Winston, Vuilleumier & Dolan, 2003; Vuilleumier et al., 2003; Vuilleumier,

Richardson, Armony, Driver & Dolan, 2004). Consistent with these fMRI findings, and important for the topic of the current thesis, a recent ERP study found that fearful faces only elicited a rapid enhancement (within 100ms) of visual brain activity in occipito-temporal areas when they consisted of LSF information (Pourtois et al., 2005). No such early enhancement of activity in visual cortex to fearful face expressions was found when faces consisted of mainly HSF. These ERP results further support the important role of LSF information in emotion expression processing and provide evidence that LSF information is of special importance during the early stages of facial expression processing (but see Holmes, Winston & Eimer, 2005).

Such rapid processing of fear based on LSF cues has been suggested to proceed through a feedback route from the amygdala to the visual areas where faces are further processed (Veuilleumier et al., 2003; Pourtois et al., 2005). The amygdala in turn receives its input from a rapid magnocellular tecto-pulvinar pathway that is preferentially tuned to processing of LSF information (Pourtois et al., 2005; Winston et al., 2003; Veuilleumier et al., 2003). The existence of such a 'subcortical face processing route' that is tuned to LSF would be consistent with anatomical evidence from animal studies that the superior colliculus and pulvinar receive substantial magnocellular inputs (Leventhal, Rodieck & Dreher, 1985; Berson, 1988; Merigan & Maunsell, 1993), and are part of a phylogenetically old route specialised for the rapid processing of fearful stimuli (Holmes et al., 2005; Le Doux, 1996).

Whereas the studies reviewed above, mainly report on processing of emotional information in the visual cortex, there are also behavioral studies that have addressed the role of SF in facial expression processing. These studies have indicated that information from different spatial frequency bands can be used flexibly for face processing (see for review Ruiz-Soler & Beltran, 2005; Sowden & Schyns, 2007). That is, the task at hand determines the usefulness of different SF scale information. . Consistent with such a flexible scale usage hypothesis, participants have for instance been shown to use LSF information to rapidly categorize emotional expressions (Schyns & Oliva, 1999) and for rapid attentional responses to fear (Holmes et al., 2005) whereas HSF information seems to be most important for the success with which one can explicitly rate emotional expressiveness (or intensity), a process that may proceed at a slower time-scale (Schyns & Oliva, 1999; Veuilleumier et al., 2003; Deruelle & Fagot, 2005; but see Goren & Wilson (2006) for different effects using synthetic faces).

One of the main problems when investigating the influence of SF on face processing is that outputs of LSF and HSF filtering differ not only at the level of the spatial scale of information they convey, but also in terms of luminance and contrast. This is related to the fact that the frequency power in natural stimuli is maximal at low SF and almost exponentially decays at higher SF (see for review Loftus & Harley, 2005). Therefore, the fast extraction of emotion based on LSF

but not HSF might be simply due to the fact that HSF stimuli are less luminant and of lower contrast. Until now, various methods have been applied to control for differences in contrast and luminance between HSF and LSF stimuli and some of them might have led to inconsistencies between the studies (see for review chapter 4). As yet, there has been no study that directly tested whether differences in contrast/luminance truly influence the processing of facial expression.

1.3 What is known about the involvement of SF in the development of facial expression processing?

As described in the previous paragraph, there is converging evidence from studies in adults for a subcortical face processing route that is rapid, operates on LSFs and modulates cortical processing. The development of this pathway has not been studied, but Johnson (2005) suggests that newborn face processing and face preferences might primarily rely on this subcortical route, or a precursor of it. This suggestion is based on evidence that face processing in newborns is primarily driven by subcortical pathways or brain structures, since the visual and other cortical areas are still relatively immature.

In addition, the infant's limited visual capacities play a role in face processing in the first year of life. The vision of a newborn is solely based on LSF information (acuity: < 1 c/d; contrast sensitivity: 0.1-0.2 c/d) (Slater & Sykes, 1977). This is caused by immaturity of the visual system at several levels, such as lower photoreceptor density and shorter segment length at the retina level, relatively less developed parvocellular neurons (compared to magno) at the Lateral Geniculate Nucleus (LGN) level and lower synaptic density and larger cortical receptive field size in the visual cortex (see for review Ellemberg, Terri, Lewis , Liu & Maurer, 1999; Hammarrenger, Leporé, Lippé, Labrossei, Guillemot & Roy, 2003). In agreement with this, a recent study by de Heering, Turati, Rossion, Bulf, Goffaux & Simion (2007) found that face recognition in newborns is primarily steered by very low SF (< 0.5 c/d) information.

However, during infancy and early childhood, the visual system develops and also other cortical areas mature. Vision rapidly increases and by the age of 3-4 years, sensitivity to HSF, as measured by the contrast sensitivity function, reaches maturity (e.g. Adams & Courage, 2002). In chapter 2 we investigate whether there are developmental differences in the type of SF that is important for facial expression processing during childhood, with an emphasis on the initial stages of facial expression processing in the brain.

1.4 Why study visual perception in Autism Spectrum Disorder?

Autism Spectrum Disorder (ASD) is a severe developmental disorder, characterized by a triad of impairments in social interaction, communication, and restricted behaviour and interests (American Psychiatric Association, 1994). The three most common forms of ASD are Autism, Asperger Syndrome and Pdd-nos. The etiology of ASD has not been clarified yet, however genetic factors are likely to play a role (Rutter, 2000). Furthermore, an increasing number of studies on ASD has led to many suggestions about possible brain abnormalities underlying this disorder. Most of these studies, however, focused on finding the brain correlates of impairments in the social domain that strongly characterize ASD. An often overlooked issue, however, is that people with ASD also show abnormalities in basic sensory processing skills. More specifically, a growing number of studies have indicated abnormalities in visual perception in ASD (see for review Dakin & Frith, 2005; Mottron, Dawson, Soulières, Hubert & Burack, 2006). Perception has been suggested to be more locally or detail oriented in ASD. This is based on a strong and still growing body of experimental evidence showing that people with ASD are characterized by superior performance on tasks that require local or detailed-focused processing and contain distracting global information, examples of such tasks are visual search tasks, embedded figure tasks and the block-design test of the WISC (see for review Dakin & Frith, 2005). A review of nearly 50 empirical studies by Happe & Frith (2006) suggests that the findings of a local bias in visual perception in ASD are robust. Clinically it has also been noted that individuals with autism often notice minor features or changes in the environment that are overlooked by others (Hayes, 1987; Kanner, 1943).

Whether global processing (e.g. the ability to see global structure by linking smaller visual elements) itself is also affected in ASD is subject of ongoing controversy. There is increasing evidence showing that people with ASD are capable of global processing (de Wit, Schlooz, Hulstijn & van Lier, 2007; Mottron et al., 2006; Rinehart, Bradshaw, Moss, Brereton & Tonge, 2000; Ozonoff, Strayer, McMahon & Filloux, 1994; Iarocci, Burack, Shore, Mottron & Enns, 2006; Plaisted, Dobler, Bell & Davis, 2006) and that deficits in performance on tasks that probe global processing in ASD are related to the local or detailed processing *bias* seen in ASD (see for review Mottron et al., 2006) as well as task instructions and complexity of the stimulus (de Wit et al., 2007; Plaisted, Swettenham, & Rees, 1999; Mottron, Burack, Stauder, & Robaey, 1999).

Importantly, the local processing style in ASD has been put forward as primary or at least contributory to some of the core characteristics of ASD, in particular problems with face processing (see for review Behrmann et al., 2006; Dakin & Frith, 2005). In agreement with this suggestion, a local bias for the

processing of faces and facial expressions has been found (Behrmann et al., 2006; Lahaie, Mottron, Arguin, Berthiaume, Jemel, Saumier, 2006; Sasson, 2006). For example, children with ASD (9 years) do not show the typical whole face advantage, i.e. superior recognition of face parts (eye, nose etc.) when they are embedded in a whole face, compared to when they are presented in isolation (Joseph & Tanaka, 2003). Furthermore, it has been found that the stronger the local bias in adults with ASD, the slower their reaction in face-based gender and identity discrimination tasks (Behrmann et al., 2006). See for similar finding with respect to emotion recognition in 8 yr-old children with ASD (Gross, 2005).

There are several theories that aim to explain the above described perceptual phenomena found in ASD (Dakin & Frith, 2005). The two main theories are the Weak Central Coherence theory (WCC) and the Enhanced Perceptual Function hypothesis (EPF). Central coherence is defined as an information processing style that is driven by a strong desire to attach meaning to what one perceives and is expressed as the tendency to process visual information in context, as a whole or overall Gestalt at the expense of details (Frith, 1989). The most recent version of the WCC suggests a lack of central coherence in ASD, causing them to perform worse in tasks in which it is important to process stimuli within a larger whole or within a context. This so-called local processing bias or cognitive style present in ASD, can be overruled by explicit task demands (Happé, 1999; Dakin & Frith, 2005; see for an updated review on WCC, Happé & Frith, 2006). At the cognitive level Happé & Frith (2006) relate WCC to difficulties in broadening the focus of visual attention. At the neural level, Happé & Frith (2006) suggest a link of WCC to reduced connectivity throughout the brain in ASD (e.g. Castelli, Frith, Happé & Frith, 2002; Just, Cherkassky, Keller & Minshew, 2004; Frith, 2003; Belmonte, Allen, Beckel-Mitchener, Boulanger, Carper & Webb, 2004; Koshino, Carpenter, Minshew, Cherkassky, Kelle & Just, 2005; Courchesne & Pierce, 2005). Both mechanisms involve deficiencies in higher-order cognitive processes such as attentional control and problems in the involvement of broader brain networks.

In contrast to the WCC theory, other theories have situated the mechanism for local bias at the level of perception (e.g. Plaisted, O'Riordan & Baron-Cohen, 1998a; Plaisted, Saksida, Alcántara & Weisblatt, 2003; Mottron et al., 2006). Plaisted and colleagues for example suggested that atypical perceptual processes in ASD might enhance the salience of individual stimulus features. Their experiments on visual search, in which participants have to search for a deviant stimulus item in an array of visual items (e.g searching for a red square between red circles an blue squares), show that ASD subjects have better search performance than controls. The authors suggest that such performance enhancement might occur at very early stages of sensory processing and may be related to an enhanced ability to discriminate between visual items (Plaisted et al., 1998a; Plaisted, O'Riordan, & Baron-Cohen, 1998b; O'Riordan, Plaisted, Driver &

Baron-Cohen, 2001; Plaisted, Saksida, Alcántara & Weisblatt, 2003; Kemner, Ewijk, van Engeland, & Hooge, 2008).

A related, though not identical 'perceptual' theory, the Enhanced Perceptual Function (EPF) hypothesis, integrates both neurophysiological and behavioral findings in ASD by adding the proposition of an over-functioning and increased autonomy (less control from higher-order areas) of brain regions that are typically involved in primary perceptual functions (see for review on the model Mottron et al., 2006). Behaviorally, this would for example be reflected in a local bias in the above mentioned visual tasks as well as superiority in discriminating low-level visual input as found by Bertone, Mottron, Jelenic, & Faubert (2005) and Plaisted et al., (1998a). Neurophysiologically, this abnormality would be reflected in enhanced sensory processing as well as a general skewing of brain activity towards primary visual areas compared to higher order visual and other cortical areas, which has indeed been found in several tasks in ASD (see for review Mottron et al., 2006).

1.5 Spatial frequency and facial expression processing in ASD

Because spatial frequencies play an important role in local-global as well as face processing in healthy adults, a few authors have put forward the hypothesis that a basic abnormality in SF processing might underlie the local processing bias seen in ASD (e.g. Boeschoten, Kemner, Kenemans, & Engeland, 2007; Deruelle, Rondan, Gepner, & Tardif, 2004). A recent ERP study indeed demonstrated abnormalities in the processing of SF in children with ASD, more specifically in the processing of HSF stimuli (gratings), originating from deviant processing in primary and secondary visual areas (Boeschoten et al., 2007). Furthermore, with respect to face processing, there is evidence that children with ASD (4-13 yrs; mean age: 6 years) primarily select HSF information for identity matching, whereas age matched typically developing children show a trend towards an LSF bias (Deruelle et al., 2004). Furthermore, a HSF bias for identity recognition has been found in a single case study on an adult with ASD, in contrast to controls who used a lower range of SFs (Curby, Schyns, Gosselin, & Gauthier, 2003). Another study indicated that adults with Asperger syndrome have difficulties in recognizing emotional expressions from very low SFs (Kätsyri, Saalasti, Tiippana, von Wendt & Sams, 2008). This preference for HSF, instead of LSF, in ASD has been suggested to be linked to a deficit of the subcortical LSF pathway for face processing (Deruelle, Rondan, Salle-Collemiche, Bastard-Rosset, & Da Fonséca, 2008; Johnson, 2005). Although speculative at this stage, such an explanation would also fit the finding that children with ASD orient less to faces early in life (Osterling & Dawson, 1994), a function thought to be primarily

steered by the LSF subcortical pathway as proposed by Johnson (2005). The experiments described in chapter 3 of this thesis will investigate whether abnormal patterns of SF processing in ASD are part of the disorder from an early age on and whether they influence facial expression processing.

1.6 Self-monitoring and ACC functioning

Whereas most studies in this thesis focus on early visual development, with increased maturation of cortical networks, deficiencies in higher order cognitive abilities are seen in ASD. One example are deficits in self-monitoring, which play an important role in social interactions (Rusell & Jarrold, 1998; Bogte, Flamma, van der Meere, & van Engeland, 2007). Self-monitoring refers to the ability to keep track of one's own actions and to evaluate whether they resulted in positive or negative outcomes in order to adapt future behavior. Abnormalities in self-monitoring might relate to problems of people with ASD to meet the requirements of social interactions. It has been suggested that if children develop difficulties in self-monitoring during childhood, they miss the normal experience of being responsible for their own actions, eventually resulting in an impoverished sense of self (Rusell & Jarrold, 1998).

Deficiencies in self-monitoring might also lead to problems in integrating self-related information with information about the behavior of other people, resulting in an atypical development of social interaction, leading to for example joint attention impairments (Mundy, 2003). Furthermore, several behavioural features in autism, like perseverative responding, repetitive behaviors, poor imitation skills, may all result from an inability to monitor ongoing behaviors and adapt behavior accordingly (Hill, 2004; Mundy, 2003; Russell, 1997; Henderson, Schwartz, Mundy, Burnette, Sutton, Zahka & Pradella, 2006).

Several studies have now indicated abnormalities in the Anterior Cingulate Cortex (ACC) in ASD, a structure in the frontal brain (e.g. Haznedar, Buchsbaum, Metzger, Solimando, Spiegel-Cohen, & Hollander, 1997; Haznedar et al., 2000). Importantly, this structure has been suggested to play an important role in the normal development of self-monitoring from late childhood to adulthood (Davies, Segalowitz, & Gavin, 2004; Ladouceur, Dahl, & Carter, 2007). In chapter 5 we investigate whether abnormal ACC functioning is related to abnormalities in self-monitoring in ASD in school age children (7-14 years; mean age: 10 years).

1.7 General aims

1) To explore the role of spatial frequency information in facial expression processing, in typically developing children at different developmental stages (3-8 years) (chapter 2).
2) To examine whether there are abnormalities in basic aspects of SF processing in young (3-4 yr-old) children with ASD compared to age and IQ matched controls, and to investigate how this affects face processing (chapter 3).
3) To investigate a methodological aspect of the role of SF in facial expression processing. More specifically, we will investigate the effect of luminance and contrast equalization on the role of HSF and LSF in facial expression processing in healthy adults (chapter 4).
4) To investigate the involvement of ACC problems in self-monitoring of actions in older children (mean age: 10 years) with ASD (chapter 5).

To address these questions the Event Related brain Potential (ERP) method is used. ERPs are derived from the electroencephalogram (EEG) that is measured continuously during execution of a perceptual or cognitive task. This is done by means of averaging activity evoked by certain types of trials (i.e. stimuli consisting of HSF or LSF information) within a certain time interval around the onset of a stimulus, in the current experiments mostly a face.

The average brain activity or brain potentials that are derived after this averaging process can be described in terms of positive and negative activity (ERP peaks) that follow each other in time and have a specific topography depending on the type of task. Such ERP fluctuations are assumed to reflect synchronized postsynaptic activity in large populations of cortical pyramidal neurons, related to sensory, motor or cognitive processes (Luck, 2005). The latency of onset of different ERP fluctuations (peaks) reflects the time course of these processes.

The first reason to use the ERP technique is that it is well suited to study influences of, for example, emotion and SF processing at different processing stages, because of its high temporal resolution. Secondly, ERPs do not require behavioral or verbal responses, and are therefore well suited for application in young children, especially when studying clinical groups.

Based on the different type of research questions the following ERP components will be examined:

The role of SF in facial expression processing in the different experiments, described in chapters 2-4, was studied by looking at the early stages of face processing in the visual areas of the brain, where interactions between SF and Emotion have been found to occur in previous studies (Pourtois et al., 2005). Two visual peaks were studied: P1 and N170. The P1 (positivity at 100

ms after Stimulus Onset (SO)) is a fast exogenous response, which reflects striate as well as extrastriate visual processing (e.g. Rossion et al., 1999). The N170 (negativity at 170 ms after SO) originates from a network of regions, probably including the fusiform gyrus, inferior occipital cortex, superior temporal sulcus and the inferior, middle and superior temporal gyri (Henson, Goshen-Gottstein, Ganel, Otten, Quayle & Rugg, 2003). The N170 is thought to be a marker of face detection, but also face encoding processes, such as the encoding of the structure or configuration of the face (e.g. position of the eyes relative to the mouth), that are important for the ability to discriminate between different faces (Jacques & Rossion, 2006).

Abnormalities in the basic aspects of SF processing in young children with ASD (chapter 3) were examined by investigating the early stages of SF processing in visual brain areas. The amplitude and latency of the visual P1 (positivity at 100 ms after SO) and N2 (negativity at 200 ms after SO) to HSF and LSF grating stimuli were examined. These peaks are both localized in visual areas and reflect striate and extrastriate visual processing. Typically, longer P1 and N2 latencies have been found when processing HSF, compared to LSF stimuli (e.g. Boeschoten et al., 2007). In addition, SF modulates the amplitude of the P1 and N2. Dependent on the exact frequency of the grating, larger amplitudes are found for HSF compared to LSF gratings on medial occipital electrodes (e.g. Boeschoten et al., 2007).

To investigate the involvement of the ACC in problems in self-monitoring in school age children with ASD (chapter 5) the latency and amplitude of two ERPcomponents, the Error-Related-Negativity (ERN; negativity around 50-100 ms after response) and Pe (error-related positivity around 200-500 ms after response) were studied. Both ERP components have been associated with self-monitoring and have been localized in the ACC in healthy adults (e.g. Hermann, Römmler, Ehlis, Hedrich, & Fallgater, 2004; van Veen & Carter, 2002). The ERN and Pe are evoked by a specific type of self-monitoring, namely response monitoring and are typically enhanced when subjects make erroneous responses during a certain task.

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An eye for detail:
An Event Related Potential study on the rapid processing of fearful facial expressions in children

2

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Child Development. (in revision)

There is converging evidence for the presence of a fast face processing route that operates on global face characteristics in the mature brain. Until now little is known about the development of such a route, which is surprising given suggestions that this fast 'global' route might be affected in neurodevelopmental disorders, such as autism. To address this, we compared early visual Event Related brain Potentials to pictures of fearful and neutral faces, containing detailed or global information in 3-4 (n= 20), 5-6 (n = 25), and 7-8 (n=25) year old children. In children, fast brain responses to emotional expressions were driven by detailed information. Developmental effects are discussed in terms of maturation of the fast route as well as increase in experience with facial expressions with age.

Chapter 2

Introduction

Decoding the emotional content of a face is an important skill in daily life, because it helps to evaluate the state and the intentions of others. Given that facial expressions like fear, anger or threat may be signals for potential danger, it is plausible that the detection and processing of emotional expression proceeds very fast. Neuroscientific studies in adults have indeed proposed a fast, phylogenetically older, route in the brain for the rapid processing of facial expressions, the so-called subcortical face processing route that includes the amygdala. This fast route is thought to bypass the slower cortical route and may directly modulate the responses of specialised visual cortical areas to faces (e.g. Le Doux, 1996; Veuilleumier, Armony, Driver & Dolan, 2003; see for review Johnson, 2005). This fast route is seen as a "quick and dirty" route which extracts emotion based on global face characteristics (the overall configuration of a face, the contours) but not detailed information, which is processed through the 'slower cortical route' (Veuilleumier et al., 2003; Johnson, 2005; Winston, Veuilleumier & Dolan, 2003; Pourtois, Dan, Grandjean, Sander & Veuilleumier, 2005). Consistent with this, several studies have found that *rapid* influences of emotional expressions on brain activity in visual brain areas as well as behavior are primarily mediated by global face characteristics rather than the details of a face (Pourtois et al., 2005; Holmes, Green & Veuilleumier, 2005; Vlamings, Goffaux & Kemner, in press). However, there are no studies that have investigated whether in children rapid brain responses to emotional expressions are also primarily mediated by global face characteristics. This is important given some theories which suggest that the fast 'global' route might be affected early in life in neurodevelopmental disorders, such as autism (Johnson, 2005; Laycock, Crewther & Crewther, 2007).

High temporal resolution Event-Related brain Potential (ERP) studies can be used to study the rapid processing of facial expressions in the brain in the order of milliseconds. Several ERP studies have reported that in both adults and children, negative facial expressions affect the amplitude and/or latency of early ERP components in visual areas. More specifically, a larger amplitude or faster latency of the P1 – a positive component that occurs over lateral visual (occipital) cortical areas, at about 100 milliseconds after presentation of a stimulus, for fearful expressions as compared to neutral or positive expressions has been noted in several studies in adults (Ashley, Veuilleumier & Swick, 2004; Batty & Taylor, 2003; Pizzagalli, Regard & Lehmann, 1999; Pizzagalli et al., 2002) as well as in infants (starting from 7 months of age) and children (Nelson and de Haan, 1996; Dawson, Webb, Carver, Panagiotides & McPartland 2004, Batty & Taylor, 2006). The latencies of these early effects are usually somewhat delayed in infants and children compared to adults.

Other studies report effects of emotional expressions on the N170 peak, which occurs about 170 milliseconds after presentation of the face stimulus and is measured at occipito-temporal electrodes. The N170 is the earliest "face-specific" ERP component, since its amplitude has been found to be consistently enhanced to *faces in comparison to multiple other, non-face, object categories* (see for review Jacques & Rossion, 2004). Typically, larger N170 amplitudes are seen in response to (negative) emotional expressions than to neutral or positive expressions in adults (Blau, Maurer, Tottenham & McCandliss, 2007; Campanella, Quinet, Bruyer, Crommelinck & Guerit, 2002; Batty & Taylor, 2003; Stekelenburg & de Gelder, 2004; De Haan, Nelson, Gunnar & Tout, 1998; Dawson et al., 2004, Batty & Taylor, 2006). In children, effects of emotional expression (negative) on the N170 have been reported in 3-4 year olds (Dawson et al. ., 2004) and 5-year-olds (De Haan et al., 1998). However, a recent study of Batty and Taylor (2006), investigating facial expression processing from early childhood to adolescence, indicated that early effects of negative emotion do not occur at the face specific N170 until the age of 14-15.

Although the P1 and N170 results are not entirely consistent across developmental studies, the above mentioned ERP studies underline the rapid (< 200 ms) processing of emotional expressions in visual areas in both adults and children. Several authors have investigated which information the visual system extracts in order to decode emotional expressions at such an early stage by manipulating the so-called spatial frequency content of face images (Veuilleumier et al., 2003; Winston, et al., 2003; Holmes, Winston & Eimer, 2005; Pourtois et al., 2005). In our everyday environment images are built up of both low- (LSF) and high spatial frequency (HSF) information, respectively referring to slow or fast luminance changes (e.g. Goldstein, 1999; de Valois & de Valois, 1988). By varying the spatial frequency content of a stimulus or image (by filtering out either high or low frequency information), one can emphasize different types of information in the image and study the difference in processing of this information (e.g. Goldstein, 1999; de Valois & de Valois, 1988). For instance, by presenting an image built up of mainly high spatial frequency, details of the image (sharp edges, contours of features such as the mouth, eyes, wrinkles etc.) are enhanced. In contrast, more global perceptual features of an image (like shading or large contours as well as the global configuration of the face: e.g. distance between eyes, eye brows and mouth) are enhanced when images are composed of mainly low spatial frequencies (Goffaux & Rossion, 2006; Morrison & Schyns, 2001).

Importantly, by varying spatial frequency information, neuroscientific studies have found evidence for differential sensitivity of the fast subcortical and slower cortical processing route to LSF and HSF information (e.g. Veuilleumier et al., 2003; Winston et al., 2003; see for review Johnson, 2005). Two fMRI studies indicated that the fast subcortical route is primarily sensitive to low spatial frequency information: enhanced activity to emotional expressions in the

amygdala and other subcortical structures was only found for faces containing LSF, but not HSF. In line with this, two ERP studies found that in adults rapid effects of emotion in visual brain areas at the P1 (Pourtois et al., 2005) and N170 (Vlamings et al., in press) are primarily mediated by LSF information, possibly through the subcortical face route (tecto-pulvinar-amygdala pathway) which is primarily sensitive to LSF and modulates activity in higher order visual face processing areas.

Behavioral studies have also provided evidence for differential sensitivity to HSF and LSF content of emotional expression for face recognition or identification in adults. For instance, it has been shown that participants use LSF information to rapidly categorize emotional expressions, whereas HSF information seems to be most important for the success with which one can explicitly rate emotional expressiveness (or intensity), a process that may proceed at a slower time-scale (Schyns & Oliva, 1999; Veuilleumier et al., 2003; Deruelle & Fagot, 2005; but see Goren & Wilson (2005) for different effects using synthetic faces). In addition, the LSF components of faces are critical to the production of rapid behavioral attentional responses towards fearful facial expressions (Holmes et al., 2005a).

Little is known about the role of low and high spatial frequencies in the perception of facial expressions in children. There is only one behavioral study (Deruelle & Fagot, 2005) which reported that 5-8 year-old children, *like adults* (Schyns & Oliva, 1999; Veuilleumier et al., 2003), rely on HSF information when explicitly processing emotional expressions from faces (deciding whether a face is smiling or not). There is, however, no information on whether the *rapid* processing of facial expressions in children is, like adults, based on LSF information. A better understanding of the normal development of facial expression processing, is also essential for the understanding of atypical development. In autism, for instance, deficiencies in the fast LSF pathway early in life have been suggested to underlie abnormalities in face processing (Johnson, 2005).

In the present study investigated effects of SF manipulations on the early processing of fearful facial expressions in the visual cortex in groups of 3-4, 5-6 and 7-8 year-old children, using the Event Related Potential technique. During a passive viewing task we examined whether the effects of emotion expression at early information processing stages (P1 and N170), are primarily mediated by global LSF cues, as in adults, or by detailed HSF information. Through administration of an additional behavioural task in which subjects were required to categorize negative (fearful) or neutral face expressions, we aimed to explore the role of spatial frequency on the maturation of more conscious emotion recognition processes. This task was only administered to the 5-6 and 7-8 year-old children.

Methods

Participants

The present study included 20 children (11 female, 9 male) between 3 and 4 years (mean age 3.10 years), 25 children (12 female, 13 male) between 5 and 6 years (mean age 6.1 years) and 25 children (12 female, 13 male) between 7 and 8 years (mean age 7.8 years). The children were recruited at an elementary school in Kerkrade (The Netherlands). The 3-4-year-old group originally counted 27 subjects, but 7 children dropped out due to ocular or muscular artefacts and/or insufficient number of trials in which they looked at the screen. In the 7-8 year-olds, three children (of 28) were excluded because they scored in the clinical range (> 63) on Internalizing (I), Externalizing (E) and Total Problem subscales of the Child Behaviour Checklist (Achenbach, 1991). The CBCL is an instrument used for the detection of behavioural problems in children and was filled in by the parents. To ensure that all children were in the normal cognitive range considering their age (IQ > 90), all 3-4 year-old children completed the SON-R 2 ½ - 7 (Tellegen, Winkel, Wijnberg-Williams, & Laros, 1998) and the 5-6 and 7-8 year-old children performed two subtests of the WISC-III (Wechsler, 1991): the block design test and vocabulary. The estimated total IQ score derived from these subtests has a mean reliability of .94 and a mean validity of .91 compared to the complete WISC-III (Spreen & Strauss, 1998).

Participants had no neurological history and had normal or corrected to normal vision. All parents gave written informed consent for participation of their child in the study. The experimental procedure was approved by a local ethical committee of the Faculty Psychology at Maastricht University, The Netherlands.

Stimuli and task procedure

Face stimuli consisted of 16 grayscale images (8 males; 8 females), one half depicting a neutral expression, the other half depicting a fearful expression. The photographs were taken from the NimStim Face Set (http://www.macbrain.org/faces/index.htm, Tottenham, Borscheid, Ellertsen, Marcus & Nelson, 2002) and have shown to evoke emotional effects at the level of the N170 before in adults (Blau et al., 2007). Face images included European-American and African-American models. Face pictures were trimmed to remove external features (neck and hairline). All pictures were fitted in a gray frame of 500 x 700 pixels. Each face subtended 6.3 degrees of visual angle at a distance of 113 cm. The HSF images were created by filtering the original photographs, using a high-pass cut-off that was ≥ 6 cycles/deg of visual angle (see figure 1). The LSF

images were created using a low-pass filter that was ≤ 2 cycles/deg of visual angle. Filtering was performed in Matlab (The Mathworks, Natick, MA) using as set of Gaussian filters.

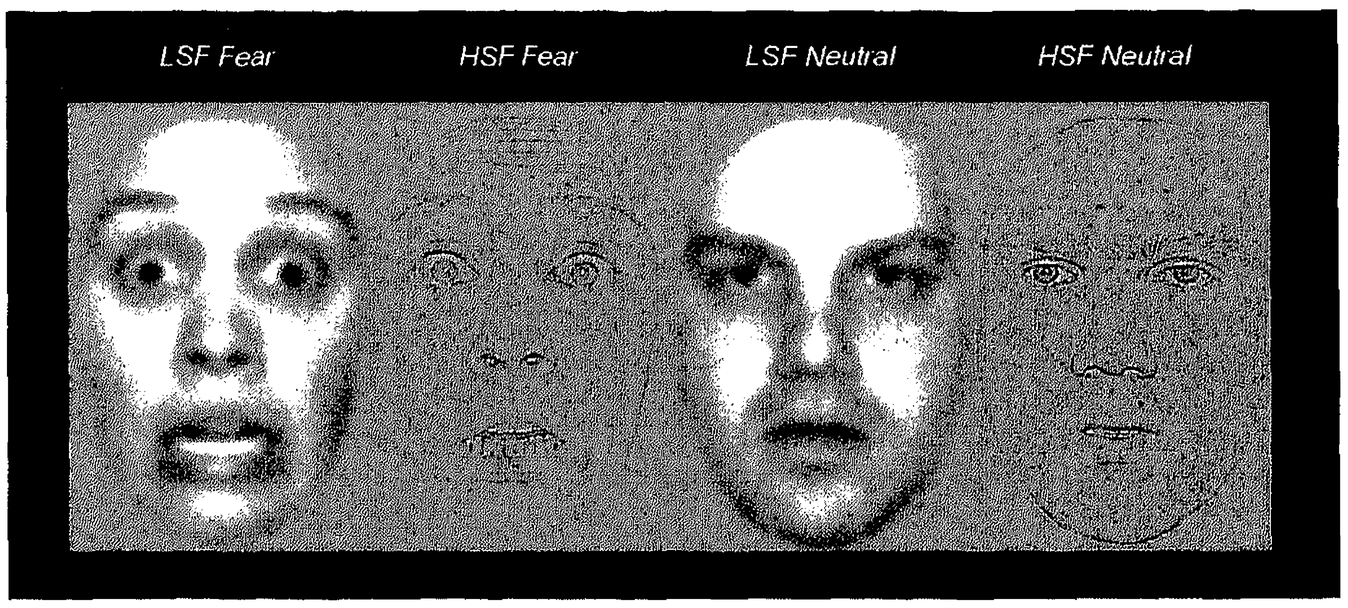

Figure 1. Example of fearful and neutral LSF (< 2 c/d) and HSF (> 6 c/d) face stimuli.

The task consisted of four blocks, each containing 73 trials. Within each block, 64 faces and 9 animation figures were presented on a grey background, in randomized order. All faces were presented for 500 ms, with an inter-stimulus interval of 1600-1800 ms. Participants were instructed to maintain fixation and to attend to all pictures. They had to press a response button as soon as they saw an animation figure on the screen and had to refrain from responding to all other images. This task was used to maintain the subject's attention towards stimulus presentation. Short pauses were given between blocks. A video camera, situated next to the screen, recorded the child's looking behaviour. For 3-4 year-olds looking behaviour was coded offline, for the 5-6 and 7-8 year-olds it was monitored online.

After the EEG measurement 5-6 and 7-8 year-old children performed an additional reaction time task in which they had to decide as fast and accurate as possible whether faces looked fearful or 'usual' ('neutral'). Presentation time and inter-stimulus intervals were kept the same as in the initial ERP task. Participants started with a practice block which contained 3 phases. In the first phase, participants were presented with a face of a lion with a fearful expression and were asked: "How does the lion look?" Incorrect answers were corrected by the experimenter. Thereafter participants were presented with a face of a lion that looked neutral and were asked: "How does the lion look?" Incorrect answers were again corrected by the experimenter. In the second phase participants were presented with a block of 32 trials in which they had to decide whether the face of the lion looked 'usual' or 'fearful' by pressing a left or right-hand button. Duration of stimulus presentation was locked to the button response. In the third phase participants had to perform the same task as in phase two, but now with

experimental task parameters: a fixed stimulus duration of as 500 ms, with a interstimulus interval of 1600-1900 ms. After the last phase participants were explained they now had to perform a similar task, which contained faces of humans instead of lion faces. Half of the stimuli (neutral) required a left button press, the other half (fearful) required a right button press. Left and right button presses were counterbalanced across subjects. The task contained the same number of stimuli (256) as the initial task ERP but was divided in 8 blocks. Furthermore no animation figures were presented between trials.

ERP Recordings

ERPs were recorded via a QuickCap containing 60 electrodes of which 37 electrodes were used. The electrodes were placed according to the 10-20 system with intermediate positions (see Fig. 2) and comprised Fp1/2, Fz, F3/4, F7/8, FC1/2, FC5/6, FT9/10, Cz, C3/4, T7/8, CP1/2, CP5/6, Pz, P3/4, P7/8, POz, PO7/8, Oz, O1/2, Iz, PO9/10 plus a ground electrode at AFz.

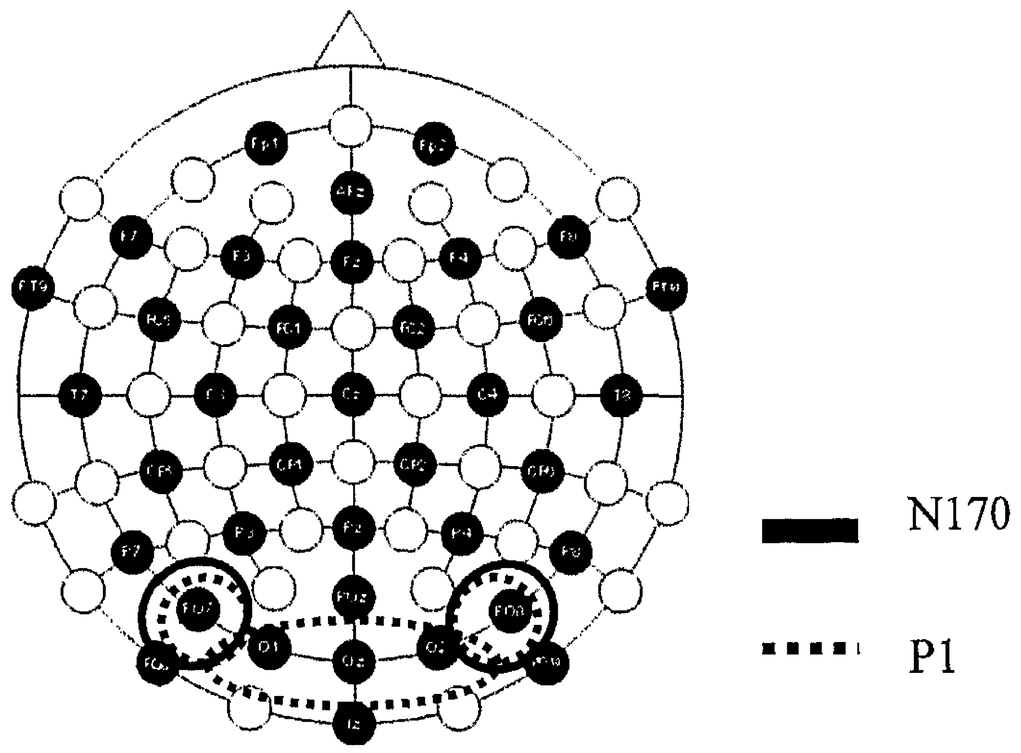

Figure 2. Scalp locations of the 36 electrodes. Mean amplitude and latency of the P1 were measured at pooled electrode sites: OZ/O1/O2/PO7/PO8. Mean amplitude and latency of the N170 was measured at occipito-temporal electrodes PO7/PO8.

Four additional electrodes placed above and below the left orbit and on the outer canthus of each eye were used to monitor vertical and horizontal eye movements. All electrodes were referenced to the left mastoid online and A2 was measured as active electrode. Impedances were kept below 20 kΩ. Continuous electroen-

cephalogram (EEG) was recorded with a 500 Hz sampling rate and a band-pass filter of 0.01-200 Hz. The EEG data was analyzed off-line using 'Vision Analyser' software (Brain Products, Munich, Germany). EEG data was epoched off-line into 1500 ms periods, starting 200 ms prior and ending 1300 ms after stimulus onset. Thereafter, the epochs were filtered (0.1-30 Hz) and artefacts from horizontal eye movements and blinks were reduced with the algorithm of Gratton, Coles & Donchin (1983). After baseline correction (-200–0), trials that contained EEG artefacts (±75 μV) were rejected from the dataset. Furthermore, trials during which the child was not looking at the screen, were discarded. Separate ERP averages were computed for all subjects, for the four stimulus conditions (SF (HSF/LSF) x Emotion (Fear/Neutral)). Finally the data were re-referenced to an average reference.

Data Analysis

Based on topographies and peak maxima (see figures 3a and 3b), regions/electrodes of interest were defined for both P1 and N170 components (see figure 2). Time windows for the components of interest were chosen through visual inspection of the grand-average waveforms in all groups (see figure 3a and 3b).To measure P1 and N170 amplitude, mean area amplitudes across a predefined time window were used instead of peak amplitudes because 1) emotional effects were present across a broader time window and did not occur at the peak only (see figure 3a and 3b) 2) mean areas are less sensitive to high frequency noise (Luck, 2005) and 3).The three groups differed in mean number of trials included in the analyses ($F(2,67) = 57.26$, $p < .001$) with fewer trials for the 3-4 year-olds (mean = 170 (SD 36)) compared to the 5-6 (mean = 243 (SD 22)) and 7-8 year-olds (mean = 243 (SD 18)). Mean areas do not become biased when the noise level increases due to different trial numbers. Consequently, it is legitimate to compare mean amplitude measurements from waveforms based on different numbers of trials, whereas this is not legitimate for peak amplitude measurements (Luck, 2005). But note that the lowest number of trials included in the analysis (170) can still be considered high. Mean amplitude of the P1 (time window: LSF: 100-160; HSF: 140-200) was extracted from a pooled set of occipito-temporal electrodes (PO7/PO8/Oz/O1/O2, see figure 2) and subjected to a 2 (SF: HSF/LSF) x 2 (Emotion: Fear/Neutral) x 3 (Group: 3-4, 5-6, 7-8 yr-olds) ANOVA. Mean amplitude of the N170 (time window: LSF: 170-270 ms; HSF: 200-300 ms) was extracted from electrodes PO7 and PO8 (see figure 2) and was subjected to a 2 (SF: HSF/LSF) x 2 (Emotion: Fear/Neutral) x 2 (Hemisphere: PO7/PO8) x 3 (Group: 3-4, 5-6, 7-8 yr-olds) ANOVA. Because the topographical distribution of the P1 did not show any laterality effects we did not include this factor in the analysis. The location from which the different components were

extracted is consistent with several ERP studies in children (see for example Dawson et al., 2004 or Batty & Taylor, 2006).

Because the grand averages (see figure 3a and 3b) showed clear effects of SF on peak latency at the P1 and N170 we also analysed peak latency for HSF and LSF. Although peak latencies, like peak amplitudes are prone to high frequency noise and have other shortcomings there are not many good alternatives and so it is often the best measure (Luck, 2005). We took the following precautions: 1) we filtered out the high-frequency noise in the waveforms (> 10 Hz) 2) used a local peak measure rather than an absolute peak measure. A local peak measure is a peak that is surrounded on both sides by smaller points. P1 latency (time window: HSF: 140-200; LSF: 140-200) was extracted from a pooled set of occipito-temporal electrodes (PO7/PO8/Oz/O1/O2, see figure 2) and subjected to a 2 (SF: HSF/LSF) x 3 (Group: 3-4, 5-6, 7-8 yr-olds) ANOVA. N170 latency (time window: 3-4 yr: LSF: 185-265 HSF: 210-290; 5-6 yr: LSF: 170-250; 200-280; 7-8 yr: LSF: 170-250; HSF: 210-290) was derived from electrodes PO7 and PO8 (see figure 2) and subjected to a 2 (SF: HSF/LSF) x 2 (Hemisphere: PO7/PO8) x 2 (Group: 3-4, 5-6, 7-8 yr-olds) ANOVA.

Reaction times (only reaction times between 150-2100 ms after stimulus onset were included in the analysis) and percentage hits from the separate categorization task were subjected to a 2 (SF: HSF/LSF) x 2 (Emotion: Fear/Neutral) x 2 (Group: 5-6 and 7-8 yr-olds) ANOVA. 4 participants (5-6 yr olds (n = 3), 7-8 yr olds (n = 1)) were excluded (significant outliers) from the analysis because they had too many misses.

When statistically significant first-, second-, or third-order interactions were found, these were further tested by looking at partial interactions in a fixed order (SF, Emotion, Hemisphere, and Group). The higher order interactions had to be significant before lower order interactions were considered. When testing of significant interactions did not lead to significant results, these were not mentioned in the paper.

Results

Grand averages and topographical distributions of the P1 and N170 are depicted in figure 3a and 3b. The means and standard errors of mean amplitude and latency measures of the P1 and N170 used for statistical analysis are depicted in figures 4 and 5.

P1 Amplitude

The overall four-way ANOVA revealed an interaction between SF and Emotion $F(1,67) = 5.42$, $p < .05$. Pairwise comparisons indicated significantly higher P1

amplitudes for fearful compared to neutral faces presented in HSF $t(69) = 2.61$, $p < .05$ (see figure 3a and figure 4), whereas the difference between neutral and fearful faces was not significant for LSF faces.

P1 Latency

The analysis of peak latency of P1 revealed a significant main effect of SF $F(1,67) = 951.915$, $p < .001$), with HSF faces showing longer P1 latencies than LSF faces (see figure 3a and figure 5).

N170 Amplitude

The overall four-way ANOVA revealed a significant interaction between SF and Emotion $F(1,67) = 9.195$, $p < .01$. As for the P1, pairwise comparisons indicated a significant effect of emotion for HSF faces only. For the N170 however, neutral HSF faces elicited significantly higher amplitudes than HSF fearful faces $t(69) = -3.673$, $p < .001$, see figure 3b and figure 4), whereas there was no effect of emotion for LSF faces.

N170 Latency

For N170 peak latency we found a significant SF x Group interaction $F(2,67) = 5.03$, $p < .01$. The SF effect was significant in each of the age groups, with LSF faces showing shorter peak latencies than HSF faces (3-4 yr-olds: $t(19) = 23.23$, $p < .001$; 5-6 yr-olds: $t(24) = 240.41$, $p < .001$; 7-8 yr-olds: $t(24) = 261.10$, $p < .001$, see figure 3b and figure 5). Further analysis revealed a significant effect of Group for LSF faces only $F(2,67) = 4.59$, $p < .05$; 3- and 4-year old children had longer N170 latencies than 7-8 year-old children $t(69) = 5.69$, $p < .05$ (see figure 3b and figure 5) when presented with an LSF face, there was no significant age difference between the younger and older age groups. Post-hoc correlation analyses indicated a significant negative correlation between age in months (including all age groups) and latency for LSF faces $r = -.28$, $p < .05$. This effect was absent for HSF faces.

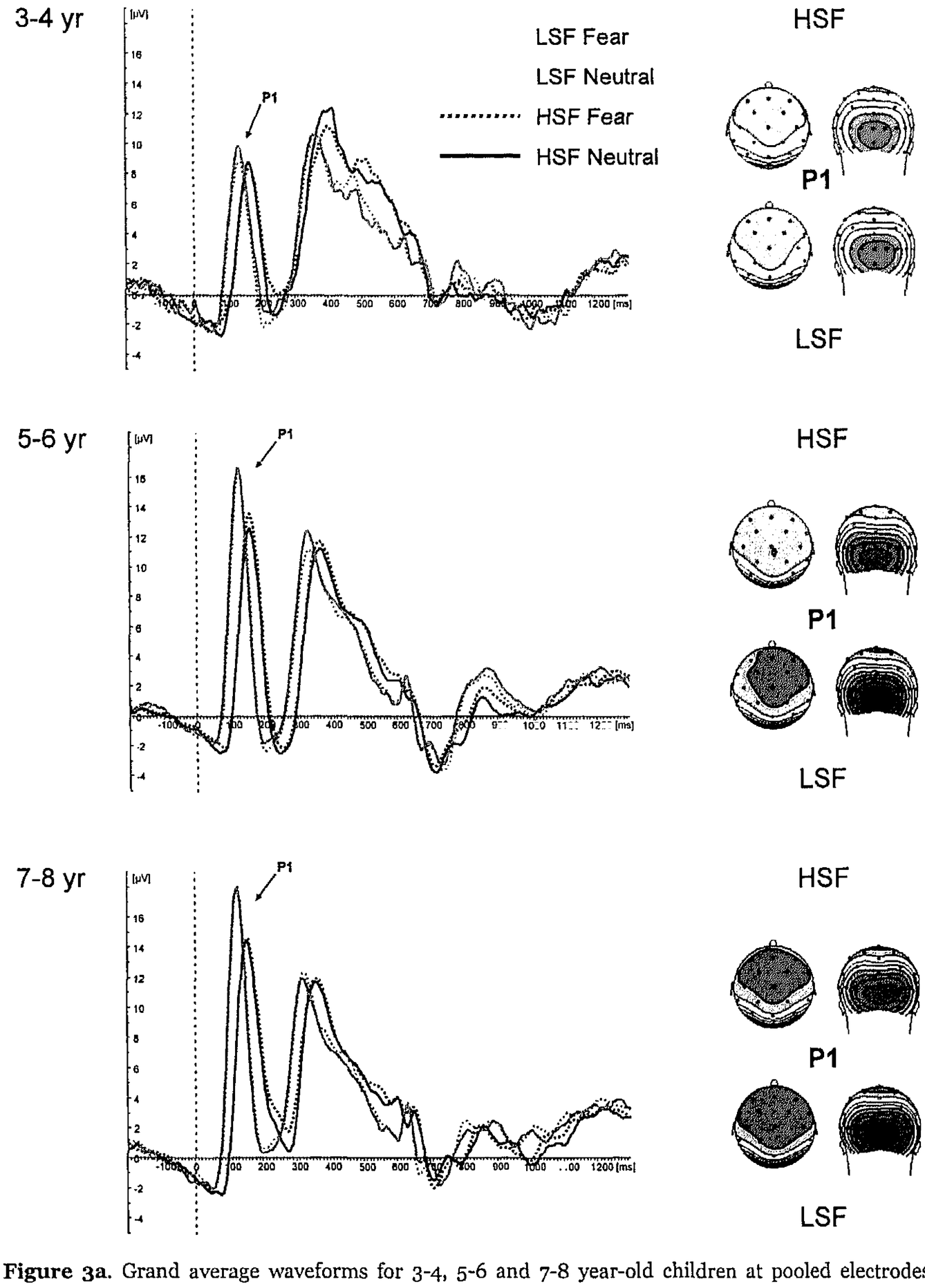

Figure 3a. Grand average waveforms for 3-4, 5-6 and 7-8 year-old children at pooled electrodes (Oz/O1/O2/PO7/PO8), from which the P1 was extracted. In addition topographical distribution of the P1 is shown. Note that because there is a difference in the way in which the grand-average waveforms (displayed in figure 3a and 3b) are calculated and the data used for statistical analysis (mean amplitudes across a predefined window, see figure 4), the values in the current graphs may differ from the values used for statistical analysis (displayed in figure 4).

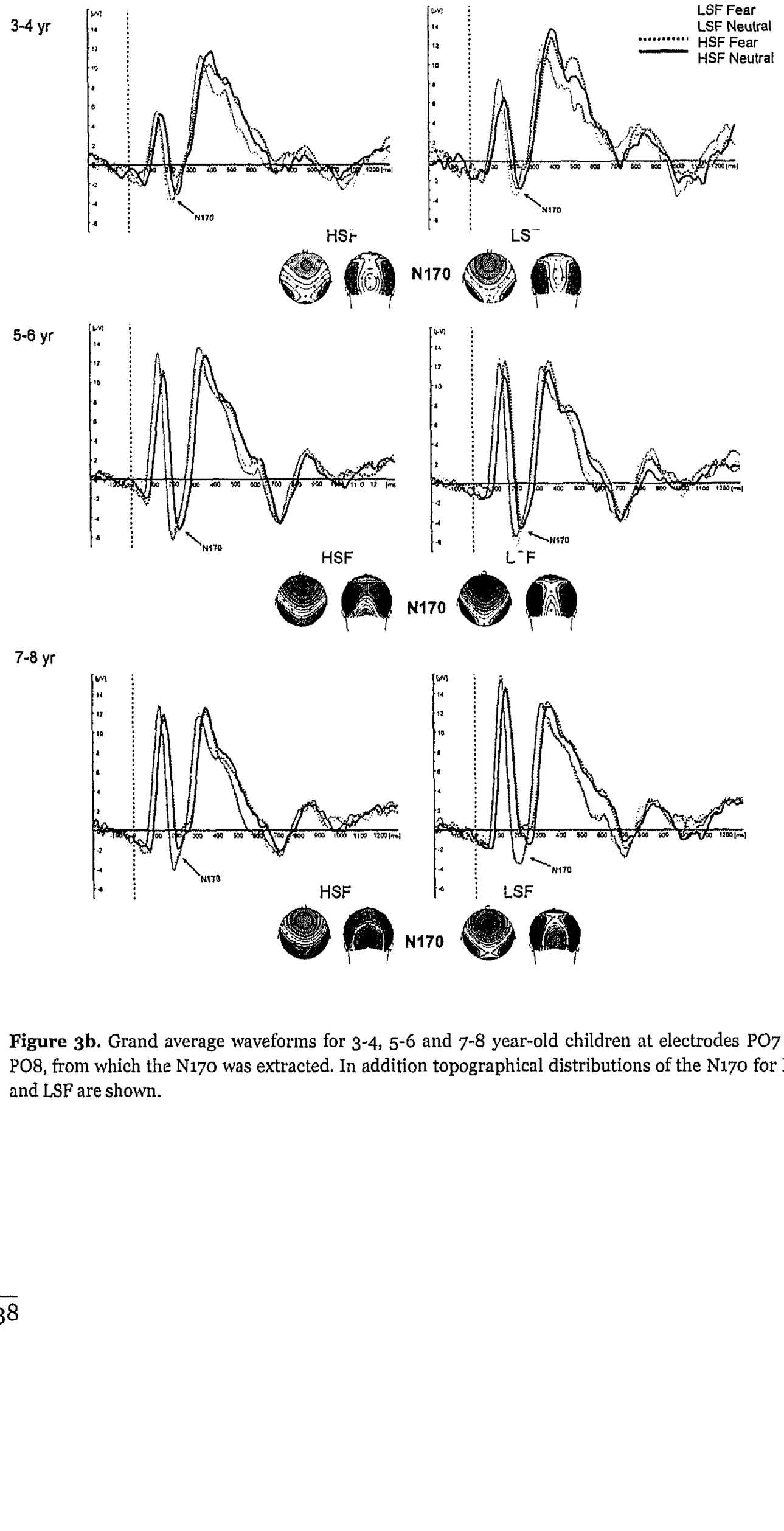

Figure 3b. Grand average waveforms for 3-4, 5-6 and 7-8 year-old children at electrodes PO7 and PO8, from which the N170 was extracted. In addition topographical distributions of the N170 for HSF and LSF are shown.

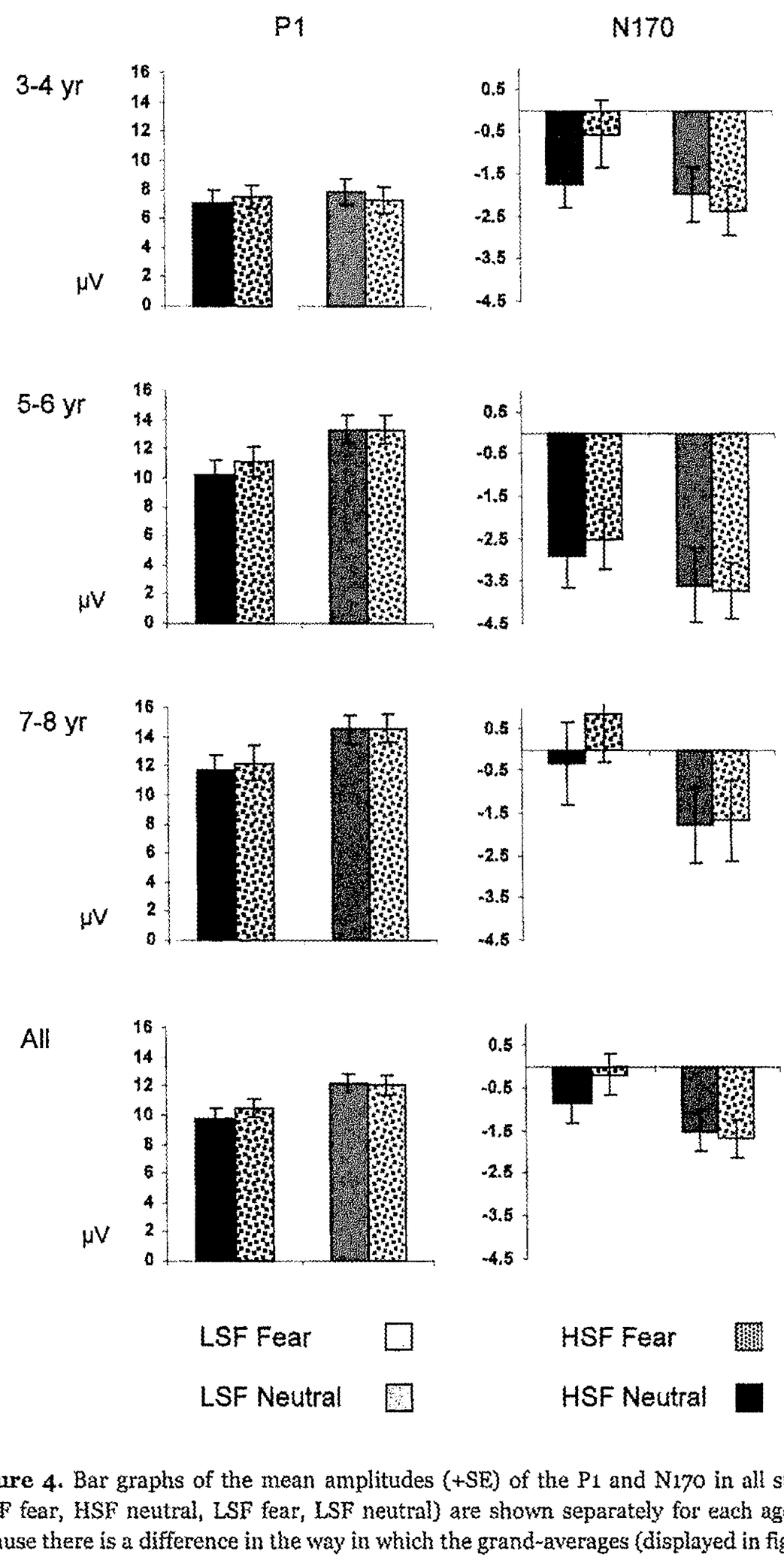

Figure 4. Bar graphs of the mean amplitudes (+SE) of the P1 and N170 in all stimulus conditions (HSF fear, HSF neutral, LSF fear, LSF neutral) are shown separately for each age group. Note that because there is a difference in the way in which the grand-averages (displayed in figure 3a and 3b) are calculated and the data used for statistical analysis, shown in the bar graphs in this figure, the values in the current graphs may differ from the values displayed in figure 3a and 3b.

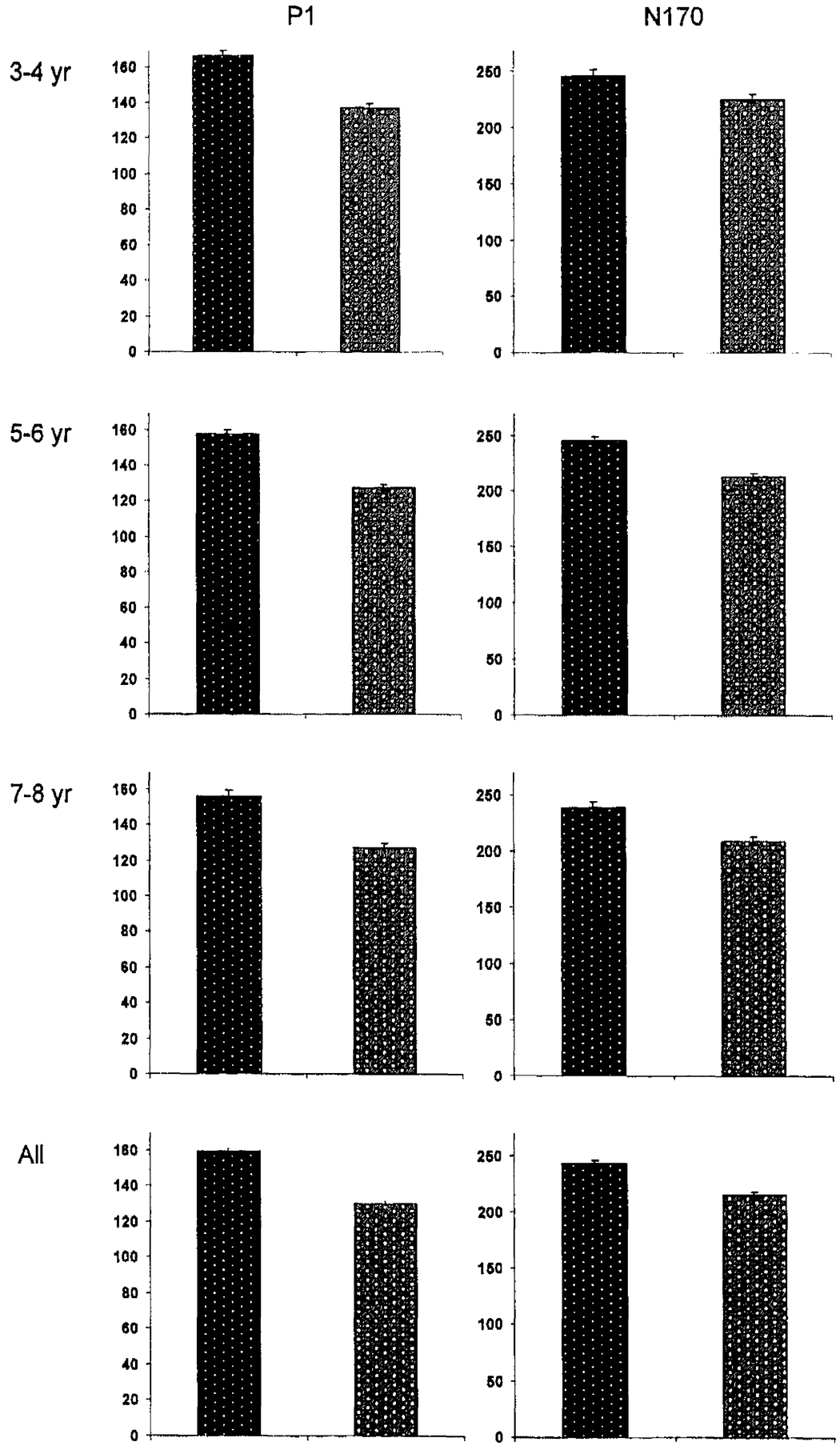

Figure 5. Bar graphs of the mean latencies in ms (+SE) of the P1 and N170 in all stimulus conditions (HSF and LSF) are shown separately for each age group.

Percentage Hits - Categorization Task

Analysis of the percentage hits recorded in the categorization task in the 5-6 and 7-8 year-olds indicated a border significant Group x Emotion interaction $F(1, 44) = 3.99$, $p = .052$; 7-8 yr olds performed slightly better on neutral compared to fearful faces $t(23) = -3.02$, $p < .01$, but there was no stimulus difference for 5-6 yr-olds. When testing group differences for neutral and fearful stimuli, 5-6 year-olds had fewer hits in the neutral condition compared to 7-8 year-olds $t(44) = .-2.58$, $p < .05$. There was a significant positive correlation between age in months and percentage of correct trials in the neutral condition $r = .35$, $p < .05$, but not in the fearful condition.

Reaction Times - Categorization Task

Analysis of the reaction times revealed a border significant effect of Emotion $F(1, 44) = 3.96$, $p = .053$, indicating faster reaction times to recognize fearful than neutral faces, see table 1. In addition, we found a main effect of Spatial Frequency $F(1, 44) = 39.69$, $p < .001$. Participants were overall faster in categorizing LSF faces than HSF faces, see table 1.

Table 1. Mean reaction times in ms (RT) and Percentage Hits (SE in parentheses) for all stimulus conditions averaged across 5-6 and 7-8 year-old children

	LSF		HSF	
	Neutral	Fear	Neutral	Fear
Hit-RT				
5-6 yr	1001 (45)	988 (44)	1030 (43)	1019 (44)
7-8 yr	986 (29)	961 (33)	1026 (31)	1002 (31)
Hit Percentage	70 (5)	75 (3)	69 (4)	72 (4)
5-6 yr	83 (3)	81 (3)	81 (3)	75 (3)
7-8 yr				

Discussion

The aim of this study was to investigate the effect of manipulation of spatial frequency content (LSF and HSF) of face stimuli on the rapid processing of negative (fearful) and neutral facial expressions in the visual cortex in childhood. To this end, early ERP components above visual cortex (P1 and N170) were measured during passive viewing of fearful and neutral face stimuli in three groups of children aged 3-4, 5-6 and 7-8 years. Recent studies revealed that in adults, early effects of facial emotion content (< 200 ms) on P1 and N170 were primarily mediated by LSF information (Pourtois et al., 2005; Vlamings et al., in press). As

was explained in the introduction, this suggests that in adults, fast extraction of a (fearful) emotional expression in visual areas might be primarily based on the processing of global face information, possibly mediated through the fast subcortical face processing route.

In contrast, in the present study we found that in children, early effects of emotion expression detection at the P1 were primarily driven by more detailed HSF information (eyes, mouth etc.). Children showed higher P1 amplitudes for fearful compared to neutral faces for HSF images only. Enhanced P1 amplitudes in response to fearful relative to neutral faces have been noted before in children and adults in studies using broadband stimuli (containing all frequencies). The higher amplitudes are typically interpreted as involuntary capture of attention towards fearful stimuli (Batty & Taylor, 2003; Pourtois et al., 2004, 2005; Williams et al., 2004; Lidell, Williams, Rathjen, Shevrin & Gordon, 2004; Eimer & Holmes, 2002; Dawson et al., 2004; de Haan & Nelson, 1996; Batty & Taylor, 2006). Additionally, present results showed that also for the face-specific N170, effects of emotional expression were only significant in the HSF condition in all children groups. The present P1 and N170 findings in the HSF condition suggest that, in contrast to adults (Pourtois et al., 2005; Vlamings et al, in press), children primarily use more detailed facial features that are represented by HSF (such as contours of the eyes, eye-brows, mouth etc.), when rapidly extracting expressions from a face.

The finding of an emotion effect for HSF, but not LSF faces, might be linked to functional changes in the emotional brain network in children. In adults, the increased P1 amplitude to fearful LSF faces has been suggested to reflect the effect of direct modulatory feedback signals on visual areas from the amygdala, which gets its input from the magnocellular pathways that are primarily sensitive to LSF (Pourtois et al., 2005). It is possible that in children the subcortical face processing route, or the fast communication between this route and cortical areas, is not fully mature. In support of this hypothesis, Cunningham, Bhattacharyya, and Benes (2002) found that amygdala-cortical connectivity continues to mature into adolescence, at least in the prefrontal areas. These suggestions are open to future investigation, possibly using fMRI.

Alternatively, the lack of emotional effects in the LSF condition in the presence of effects in the HSF condition might be explained by less face expertise in children. An interaction between experience and spatial frequency has been noted before in a behavioural study on tool expertise (Viggiano, Righi & Galli, 2006). Viggiano et al. (2006) showed that in tool-experts, who have experienced prolonged exposure to tools, a small amount of LSF information in tool pictures was sufficient for tool identification in contrast to novices who performed best for stimuli containing HSF information. With respect to face processing there have been no studies yet directly investigating this interaction between expertise and spatial frequency. However, several studies have now suggested stronger

configural processing (i.e. larger inversion effect) for face stimuli for which participants have expertise (see for review McCleery et al., 2008; Parr & Heintz, 2008). Importantly, low spatial frequencies play an important role in configural face processing (Flevaris, Robertson & Bentin, 2008; Goffaux, Hault, Michel, Vuong & Rossion, 2005; Goffaux, Gauthier & Rossion, 2003). Maybe with more expertise with different facial expressions and faces in general, HSF effects in children disappear and LSF information might start to dominate early effects of emotion processing at the P1 and N170.

Surprisingly, the HSF emotion effect at the N170 was opposite to that of the P1. At the P1, the data suggest increased processing of fearful stimuli, while at the N170, amplitudes were larger to neutral than fearful stimuli in all 3-8 year-old children. A possible explanation for these N170 findings might be that in children, specialised face processing areas do not process 'neutral' faces as emotionally neutral. In a recent study Durand, Gallay, Seigneuric, Robichon, and Baudouin (2007) showed that the ability to recognize neutrality in faces continues to develop until 9 years of age. Below 9 years, children had the tendency to attribute an emotion (happiness or sadness) to neutral faces (see also Carlson, Felleman & Masters, 1983; Felleman, Barden, Carlson, Rosenberg & Masters, 1983; Reichenbach & Masters, 1983). In the categorization task in the present study, a developmental effect was shown as well by the fact that the oldest (7-8 yr-old) children in our study correctly categorized a higher percentage of neutral faces than 5-6 year-olds. Supporting the above mentioned studies Thomas et al. (2001) demonstrated even greater amygdala activity to neutral faces than fearful faces in children, whereas adults showed enhanced activity to fearful faces (see also Tottenham, Hare & Casey, in press).

Thomas and her colleagues (2001) argue that this difference between adults and children may be present because children observe neutral faces as being more ambiguous than fearful faces. Neutral facial expressions might not yet represent neutrality for children, and enhanced activity to neutral broadband faces may be produced by enhanced effort invested in trying to decode or interpret the expression. Such an explanation would be congruent with the fact that in the present study amplitudes to neutral faces were only enhanced for the N170 and not the P1. As opposed to the P1, that is assumed to be primarily sensitive to low-level visual processing or attentional manipulations, the N170 is thought to be especially involved in structural encoding of faces (Jacques & Rossion, 2006; Taylor, 2002; Valdes-Sosa, Bobes, Rodrigues & Pinilla, 1998; Nobre, Rao & Chelazzi, 2006).

With respect to the latency of the P1 and N170, we found faster latencies for processing of LSF compared to HSF stimuli, irrespective of facial expression. This is consistent with several electrophysiological face studies reporting similar effects in adults (McCarthy, Puce, Belger & Allision, 1999; Halit, de Haan, Schyns & Johnson, 2006; Hsiao, Hsieh, Lin & Chang, 2005) as well as visual evoked

potential studies in adults that reported SF effects on ERP latency for non-facial stimuli (Mihaylova, Stomonyakov & Vassilev, 1999; Musselwhite & Jeffreys , 1985). This temporal precedence of LSF compared to HSF is consistent with previous findings that the neuronal pathways sensitive to LSF and HSF have dissociable time scales with faster cortical arrival of information that was processed in the parvocellular (mainly sensitive to HSF due to small receptive field size) compared to the magnocellular (mainly sensitive to LSF due to large receptive field size) system (Maunsell et al., 1999; Schroeder, Tenke, Arezzo & Vaughan, 1989; Bullier, Schall & Morel, 1996; Klistorner, Crewther & Crewther, 1997; see for review Laycock et al., 2007). Importantly, with increasing age the latency of the N170 decreased in the LSF condition whereas there were no significant age effects for processing of HSF faces. Faster N170 latencies with increasing age have been reported before for stimuli faces containing both high and low SF information (see for review Taylor, Batty & Itier, 2004). The present study thus suggests that this decrease in N170 latency to unfiltered faces might be caused specifically by faster extraction of LSF information (overall face configuration, contours etc.).

Finally, in a behavioural task we investigated whether an LSF/HSF advantage for the processing of facial expressions would be reflected in reaction times to an active categorization task. Like in adults (Vlamings et al., in press), children showed an effect of emotional expression irrespective of SF. Children decided more quickly that a face was fearful than that it was neutral, which is consistent with the finding that stimuli that signal threat receive preferential attention over neutral stimuli (see for review Holmes et al., 2005a). The lack of an interaction between emotion and SF suggests that in the later stages of information processing (at response level), emotional expressions are recognized based on LSF as well as HSF information. Children showed faster processing of LSF over HSF stimuli, which is consistent with several other behavioural studies (Coin, Versace & Tiberghien, 1992; Parker, Lishman & Hughes, 1992; 1997) that found faster processing of LSF information.

In conclusion, the present data show that in contrast to adults, in children early effects of facial expression in the visual cortex at the P1 and N170 are primarily mediated by HSF cues (eyes, mouth etc.). Emotional effects (difference between neutral and fearful face expressions) were, however, different for P1 and N170. In all children, P1 amplitude was enhanced in response to HSF fearful relative to neutral faces, whereas N170 amplitude was enhanced to HSF neutral (vs fearful) faces. In agreement with earlier work (Carlson, Felleman & Masters, 1983; Felleman, Barden, Carlson, Rosenberg & Masters, 1983; Reichenbach & Masters, 1983; Durand et al., 2007), the latter data indicate that neutral faces might have an ambiguous character for young children, as supported by increased error rates for neutral faces. P1 and N170 responses were not different for fearful or neutral expressions for LSF images, which might be related to im-

mature functioning of the rapid subcortical route for face processing which includes the amygdala and gets its input form magnocellular pathways (Johnson, 2005). Finally, our data suggest that a developmental latency decrease of the N170 could be linked to faster extraction of LSF cues with age. The present data might be important for research in psychiatric disorders like autism, for which specific deficits in the processing of LSF have been suggested (see for review Johnson, 2005; Laycock et al., 2007).

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Spatial frequency processing in young children with Autism Spectrum Disorder

3

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in preparation

Input to the visual system is built up of both low- (LSF) and high spatial frequency (HSF) information. HSF represent, small luminance changes, corresponding to fine perceptual detail. LSF represent global changes in luminance, and provide information about the general shape of objects. Especially LSF have been shown to play an important role in facial expression processing. Interestingly, in ASD a more detailed visual processing style has been noted and some studies have suggested that this is related to abnormal SF processing.

In the present study we investigated whether abnormalities in SF processing are present at an early age in ASD and whether they contribute to abnormalities in face processing, more specifically the processing of facial expressions. Twenty two 3-4-year-old children with ASD were compared with seventeen developmentally delayed, but non-autistic children. Children watched HSF and LSF grating patterns and pictures of neutral or fearful faces, with either a HSF or LSF content. During picture presentation brain activity was measured, using event-related brain potentials .

Results showed enhanced activity to HSF compared to LSF grating patterns in young children with ASD, in contrast to controls. Importantly, abnormal SF processing was also reflected in the processing of facial expression in ASD. Facial expression processing was primarily driven by HSF in ASD, in contrast to controls.

The present data indicate that enhanced activity to HSF information is present early in life in ASD. Furthermore, our results suggest that the fast face processing route, which is preferentially tuned to LSF information and also responsible for face orienting in infancy, is affected in ASD at an early age.

Chapter 3

Introduction

Recent advances in autism research indicate that besides having difficulties in social interaction and communication, people with autism perceive the world differently. More specifically, a growing number of studies have indicated abnormalities in visual perception in ASD (see for review Dakin & Frith, 2005; Happe & Frith, 2006; Mottron, Dawson, Soulières, Hubert, & Burack, 2006; Behrmann, Thomas, & Humphreys, 2006). Several studies have now robustly demonstrated enhanced performance in visual search, detection of hidden figures, and learning of highly confusable patterns (e.g. Caron, Mottron, Barthiaume, & Dawson, 2006; Happe & Frith, 2006; O'Riordan, Plaisted, Driver, & Baron-Cohen, 2001; Plaisted, O'Riordan, Baron-Cohen, 1998a, Plaisted, O'Riordan, Baron-Cohen, 1998b). Additionally, exceptional abilities haven been noted involving focus on detailed information (Mottron & Belleville, 1993; Mottron et al., 2006). Based on these findings, perception has been suggested to be more locally or detail oriented in ASD (see for review Dakin & Frith 2005; Mottron et al., 2006; Behrmann et al., 2006). Importantly, this local processing style in ASD has been put forward as primary or at least contributory to problems in the processing of faces, which play a crucial role in social communicative development (e.g. Deruelle, Rondan, Salle-Collemiche, Bastard-Rosset, & Da Fonséca, 2008; Curby, Schyns, Gosselin, & Gauthier, 2007; de Jong, van Engeland, & Kemner, 2008, Deruelle & Fagot, 2005; Deruelle, Rondan, Gepner, & Tardif, 2004; Behrmann et al., 2006). Recently the local bias has been related to abnormalities in low-level perception in ASD (see for review Mottron et al., 2006). However, until now there are no studies that have investigated whether abnormalities in low-level perception are part of Autism Spectrum Disorder from an early age on. In the present study we will investigate one of the most fundamental aspects of low-level visual perception, namely spatial frequency processing, in very young children with ASD.

Input to the visual system from our everyday environment is built up of both low- (LSF) and high spatial frequency (HSF) information (e.g. Goldstein, 1999; de Valois & de Valois, 1988). High spatial frequencies represent abrupt, small luminance changes, corresponding to sharp edges and fine perceptual detail. Low spatial frequencies on the other hand represent global changes in luminance, and provide information about the general shape, proportions and large contours of objects in our visual environment (Bar, 2004; Goffaux & Rossion, 2006; Morrison & Schyns, 2001). The differential processing of HSF and LSF processing by the visual system plays a central role in face processing (see for review Ruiz-Soler, 2005; Goffaux & Rossion, 2006). By manipulating the spatial frequency content of face images, several studies have indicated that the visual system is able to rapidly and efficiently process faces at a single glance (holistically) based on LSF information (see for review Goffaux & Rossion, 2006). In

addition, there is converging evidence for the presence of a fast processing route for the processing of emotional expressions that is preferentially tuned to LSF and is fed by magnocellular input (Pourtois, Dan, Grandjean, Sander, & Veuilleumier, 2005; Vuilleumier, Armony, Driver, & Dolan, 2003; Winston, Vuilleumier, & Dolan, 2003; Holmes, Green, & Vuilleumier, 2005; Johnson, 2005).

Because of its important role in face processing, a few studies have investigated whether there is an abnormality in spatial frequency processing in individuals with ASD (Boeschoten, Kenemans, van Engeland, & Kemner, 2007; Deruelle et al., 2004; Deruelle & Fagot, 2005; Deruelle et al., 2008 ; Curby et al., 2007). Interestingly, and consistent with previous reports of locally oriented perception in ASD, several studies found atypical processing of high spatial frequencies in ASD. For instance Boeschoten et al. (2007) found abnormalities in HSF processing in the early stages (< 200ms) of visual processing as reflect by Visual Evoked Potentials (visual ERPs) in children (mean age: 10 years) with ASD. In addition, a number of behavioral studies demonstrated that in contrast to controls, face perception was guided by HSF in children and adults with ASD in tasks measuring identity and emotion recognition (Curby et al., 2007; Deruelle et al., 2004; Deruelle & Fagot, 2005; Deruelle et al., 2008). Several authors hypothesized that the fast face processing route that is preferentially tuned to LSF, is affected in ASD (Laycock, Crewther, & Crewther, 2007; Johnson; 2005; Deruelle et al., 2008).

In the present study we investigate *within* one study 1) whether basic abnormalities in spatial frequency processing, as reflected in electrical brain activity above the visual areas, are already present at a very young age (3- 4 years) in ASD and 2) how spatial frequency influences the rapid processing of emotional expressions in this age group. We predict basic abnormalities in HSF processing as reflected by the amplitude and latency of different VEP peaks (P1 and N2) to grating stimuli, that reflect striate and extrastriate sensory processing. Grating stimuli are patterned stimuli that are typically used to investigate the fundamentals of spatial frequency processing (Kenemans, Baas, Mangun, & Verbaten, 2000; Boeschoten et al., 2007). In addition, we predict that effects of emotion on the amplitude of different ERP components to facial images (P1 and N170) are primarily driven by LSF in controls and HSF in children with ASD.

Methods

Participants

Two groups of children participated in the present study: 29 children diagnosed with Autism Spectrum Disorder (ASD) and 18 control children with a developmental delay without ASD. Participants were recruited from Karakter, University

Center for Child and Adolescent Psychiatry in Nijmegen, the Department of Child and Adolescent Psychiatry from University Medical Center Utrecht (ASD group) and Medical Child day care centers in Maastricht, Heerlen and Utrecht (control group). Exclusion criteria for all children were a history of serious head injury, seizures, epilepsy and medication. Seven ASD children (of 29) were excluded because they were not compliant with the ERP procedure and one control child who was on medication. The final group consisted of 22 children with ASD and 17 controls. All children had normal or corrected to normal vision.

The diagnosis of ASD (either autism (n = 15) or pdd-nos (n = 7), no comorbidities) were made by a psychiatrist based on DSM-IV criteria (American Psychiatric Association, 1994). In addition, all children met the criteria for ASD on the: Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter, & Le Couteur, 1989) (except for one child where the ADI was not administered) and the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1989). Both the ADI and ADOS were administered by a trained rater. See table 1 for average scores on the ADI-R and ADOS.

Additional exclusion criteria for the control group were the presence of a diagnosis or suspicion of ASD, ADHD, Childhood Disintegrative disorder, Fragile X, Klinefelter and Rett-disorder. In addition, to check for the presence of autistic symptoms in the control group, parents filled in the Social Emotional Questionnaire (Rutter, Bailey, & Lord, 2003), which is based on the ADI. None of the control children scored above the cut-off for autism (the SEQ was not filled in for one child).

Groups did not differ in sex, chronological age, performal or verbal age (see table 1). Nonverbal mental age was quantified by either the SON-IQ test (Tellegen, Winkel, Wijnberg-Williams, & Laros, 1998), average of the non-verbal scales of the WIPSI (Wechsler, 1991), Mullen (1995) or PEP (Schopler, Reichler, Bashford, Lansing, & Marcus, 1990). Verbal mental age was quantified by the Reynell test for language (Reynell & Huntly, 1985), an average of the verbal scales of the WIPSI (Wechsler, 1991), verbal scales of the Mullen (Mullen, 1995) or the cognitive verbal scale of the PEP (Schopler et al., 1990). The experiment was approved by the Medical Ethical Committee of the Radboud Hospital in Nijmegen and all parents gave written informed consent before participation.

.ble 1. Descriptive data for ASD children and controls

riable		ASD (n = 22)	Controls (n = 17)	T and p-values
ıle (female)		18 (3)	17(12)	t (37) = 1.15; p = 25
٨ (months)				
Range		35-60	36-67	
Mean ± SE		48.4 ± 1.3	51.6 ± 2.6	t (37) = 1.12, p = .28
ɔn-verbal MA				
Range		18-61	19-60	
Mean ± SE		37.4 ± 2.7	35.9 ± 2.5	t (37) = -.40, p = .69
:rbal MA				
Range		8-63	11-70	
Mean ± SE		35.5 ± 3.6	36.5 ± 3.8	t (37) = -.20, p = .84
DI-R score ± SD				
Social Behavior	(cut-off = 10)	14.3 ± 6.4	NA*	
Communication	(cut-off = 8)	10.1 ± 4.4	NA	
Repetitive Behavior	(cut-off = 3)	4.1 ± 2.8	NA	
DOS scores ± SD				
Communication	(cut-off = 2)	3.7 ± 2.0	NA	
Social Behavior	(cut-off = 4)	8.3 ± 2.8	NA	
inical Diagnosis				
Pdd-nos		7		
Autism		15		

NA: Not Asked

'timuli and task procedure

'he grating and facial emotion task were administered in separate sessions (session 1: gratings task; session 2: facial emotion task). Four ASD children only articipated in session 1. Testing took place in a quit room, where children were ositioned in a comfortable chair or on their parents lap (depending on child's reference) at 113 cm from the screen with the monitor fixed at eye level.

Grating task: Horizontal (square-wave) black-and-white gratings with either HSF (6 cycles per degree (c/d)) or a LSF (0.75 c/d) (see figure 1) were presented on a computer with a duration of 500 ms. The task consisted of three locks containing 60 trials each (30 HSF and 30 LSF). The contrast of all gratngs was 100 % (Michelson fraction), their luminance was 44 cd/m² and the size vas 5.3 degrees of visual angle. To motivate the children to attend the stimuli, in ddition, each block contained 10 different moving and coloured animations (10 ɔer block; duration: 2000 ms), which clearly differed from the grating stimuli. ٨ll stimuli were presented randomly against a grey background with an inter-

stimulus interval that varied between 500 and 1000 ms. Participants were instructed to attend to all pictures and to respond to all animations with a button press. No responses were required for the the stimuli of interest, the gratings. After a hit (button press within 3000 ms after onset) a happy sound (Yoohoo-hoohoo) was presented, after a miss, a negative sound (boing) was played. At the beginning of the session there was one practice block containing 48 trials and 5 animations. If children were not able to perform the task themselves, their parents were asked to push the response button, to keep the motivating auditory stimulation. In this case children always sat on their parents lap. There were no group differences in the number of children that were able to actively perform the task (controls: 70%; ASD: 64%; ($t(37) = .45$, $p = .65$)). The active task (pushing the response button on animation onset) was only included to increase children's attention at the screen. A pilot study using a fully passive task indicated that children were easily distracted.

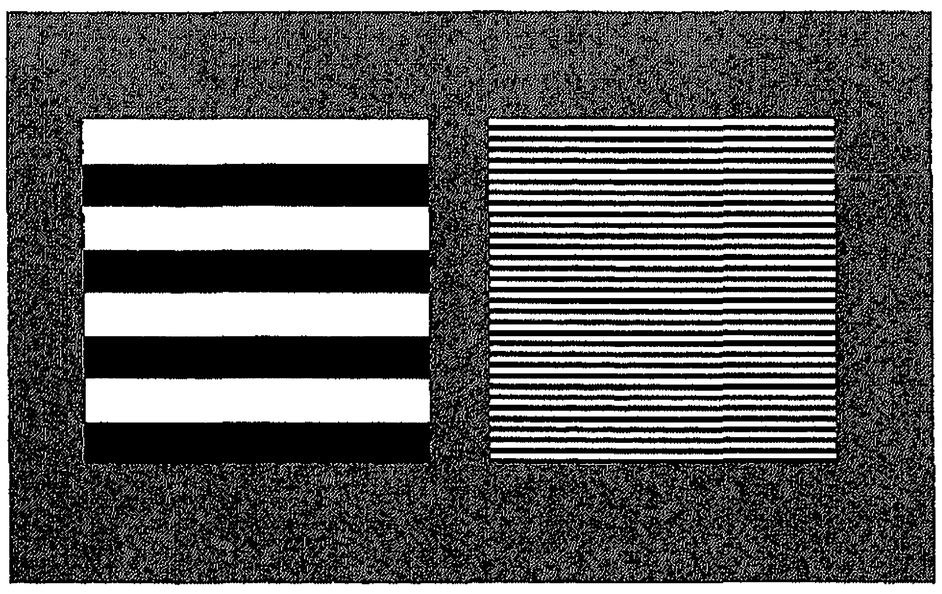

Figure 1. The grating stimuli used in this study.

The facial emotion task: Filtered face stimuli were presented, consisting of 16 grayscale images (8 males; 8 females), one half depicting a neutral expression, the other half depicting a fearful expression. The photographs were taken from the NimStim Face Set (http://www.macbrain.org/faces/index.htm, Tottenham, Borscheid, Ellertsen, Marcus & Nelson, 2002). Face images included European-American and African-American models. Face pictures were trimmed to remove external features (neck and hairline). All pictures were fitted in a gray frame of 500 x 700 pixels. Each face subtended 6.3 degrees of visual angle at a distance of 113 cm. The HSF images were created by filtering the original photographs, using a high-pass cut-off of ≥ 6 cycles/deg of visual angle for the HSF stimuli, and a low-lass filter of ≤ 2 cycles/deg of visual angle for the LSF stimuli (see figure 2).

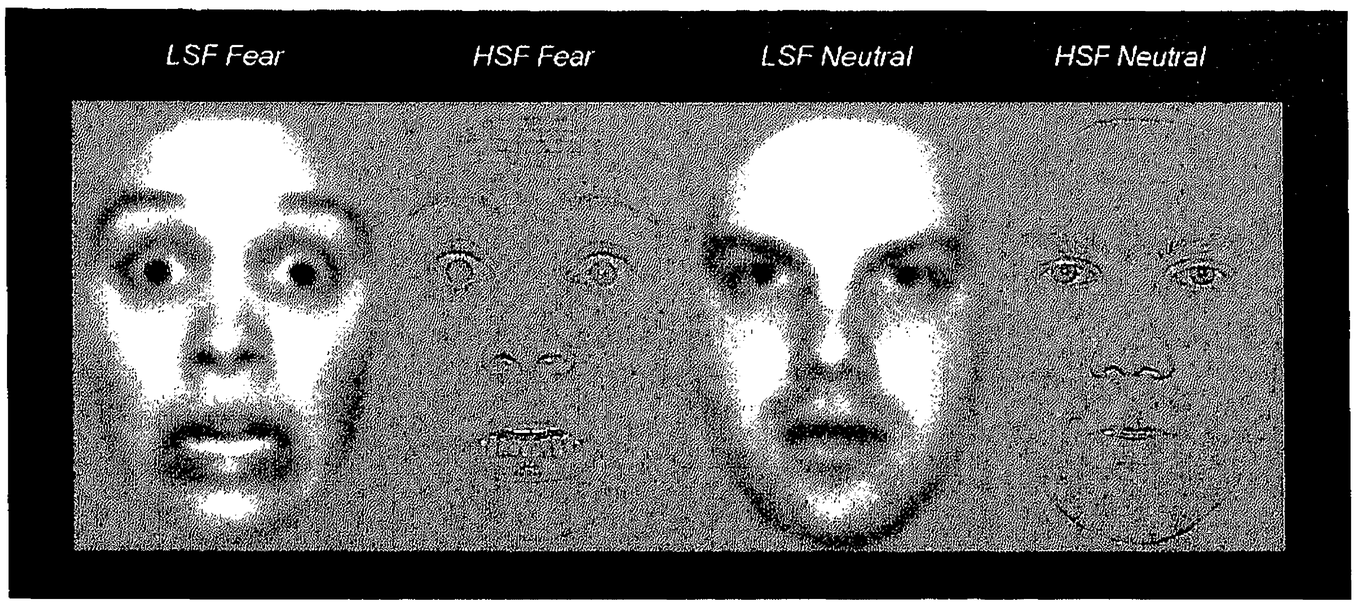

Figure 2. Example of fearful and neutral LSF (< 2 c/d) and HSF (> 6 c/d) face stimuli.

Filtering was performed in Matlab (The Mathworks, Natick, MA) using as set of Gaussian filters. The facial emotion task consisted of four blocks, each containing 73 trials. Within each block, 64 faces and 9 animation figures were presented on a grey background, in randomized order. Also analogous to the grating task, 9 animation figures were included in each block, to which the children had to react with a button press. All faces were presented for 500 ms, with an inter-stimulus interval of 1600-1800 ms. There were no group differences in the number of children that were able to actively perform the task (controls: 75%; ASD: 87% $t(29) = -.80$, $p = .43$).

To monitor the child's looking behaviour all children were video-taped. A pile containing 3 vertically positioned green led lights was positioned next to the child. At stimulus onset one of the led lights or a combination of led lights illuminated and signalled the type of stimulus that was presented (e.g. upper and middle led light = HSF neutral face). A camera, positioned next to the monitor, filmed the child's face as well as the pile with the led light. By coding of the videos after testing, trials at which children looked away from the screen (at stimulus onset) could be traced. Children were rewarded for participation with a small present.

ERP Recordings

ERPs were recorded via an EasyCap containing 39 electrodes. 36 electrodes were placed according to the 10 % system (equidistant electrodes) Fp1/2, AFz, Fz, F3/4, F7/8, FC1/2, FC5/6, FT9/10, Cz, C3/4, T7/8, CP1/2, CP5/6, TP9/TP10, Pz, P3/4, P7/8, POz, O1/2, Iz, PO9/10. To fully cover our region of interest, the visual areas, we added three extra electrodes (PO7/PO8, OZ). Afz served as the ground electrode. Additionally, four electrodes placed above and below the left orbit and on the outer canthus of each eye were used to monitor vertical and horizontal eye movements. All electrodes were referenced to the left mastoid

online and a second electrode positioned at the right mastoid was measured as an active electrode. Impedances were kept below 20 kΩ.

EEG was recorded with a 500 Hz sampling rate and a band-pass filter of 0.01-200 Hz. The EEG data was analyzed off-line using 'Vision Analyser' software (Brain Products, Munich, Germany). EEG data was epoched off-line into segments starting 200 ms prior and ending 800 ms in the grating task and 1300 ms after stimulus onset in the face task. Thereafter, the epochs were filtered (0.1-30 Hz) and artefacts from horizontal eye movements and blinks were removed using the algorithm of Gratton, Coles & Donchin (1983). After baseline correction (200 ms before stimulus onset), trials that contained EEG artefacts (± 100 μV) were rejected from the dataset. Furthermore trials during which the child did not look at the screen at stimulus onset, were discarded. During the grating task of one child with ASD and the facial emotion task of one control child and one child with ASD the led lights did not function. However, review of the videos indicated that both children paid sufficient attention to the task. In the gratings task, all children passed the criteria of 25 trials per condition after rejection of artefacts and trials of inattention. There were no significant group differences in the number of trials included in the analysis ($t(37) = 1.61$, $p < .12$). In the face task three ASD children and one control did not pass the criterion of twenty five trials per condition (HSF fear, HSF Neutral etc.) to be included in the analysis. Interestingly, we observed a significant negative correlation between number of trials children with ASD looked at the screen in the face task and level of social behaviour ($r(17) = -.62$, $p < .01$) and communication ($r(17) = -.61$, $p < .05$) as measured by the ADOS. There were no correlations between looking behaviour and ADOS measures in the grating task. After exclusion of the above mentioned children, groups did not differ in number of trials included in the analysis of the facial emotion task ($t(29) = .34$, $p = .74$). Neither did the groups differ in sexe, chronological-, mental- or verbal age. Separate ERP averages were computed for all subjects, for the stimulus conditions of interest (Gratings task: HSF/LSF; Facial emotion task: HSF neutral; HSF fear; LSF neutral; LSF fear). Finally, the data were re-referenced to an average reference.

Data Analysis

With respect to the grating task, we tested whether there are between group differences in SF processing as reflected by the amplitude and latency of different VEP peaks (P1 and N2) to grating stimuli, as effects of SF on these parameters are typically seen in healthy adults SF.

With respect to the facial emotion task, our main interest was whether there was a difference between groups in facial expression processing in each of the two SF categories To investigate this we examined early facial expression proc-

essing as indexed by P1 and N170 amplitude, as effects in earlier studies in adults were seen for amplitude only (see also Pourtois et al., 2005; Vlamings, Goffaux & Kemner, in press).

Grating task: Peak latency and amplitude of the P1 and N200, were extracted from occipital electrodes Oz, O1 and O2 (see figure 3 and 4), at which these components reached peak maxima. The time windows for peak scoring were based on visual inspection of the grand-averages: P1 (LSF: 80-150; HSF: 100-170) and N200 (LSF: 170-300; HSF: 200-300). The mean peak latencies and amplitudes were calculated as the mean of the individual peaks over the three electrodes and were subjected to a 2 (SF: HSF; LSF) x 2 (Group: controls; ASD) ANOVA. When statistically significant interactions were found, these were further tested, using planned comparisons. When testing of such interactions did not lead to significant results, these were not mentioned in the paper.

The facial emotion task: amplitude of the P1 were measured at electrodes OZ, O1, O2, PO7 and PO8 and peak latency and amplitude of the N170 were extracted from temporal electrodes P7, P8, PO7 and PO8, at which these components reached peak maxima. To measure P1 and N170 amplitude, mean amplitudes across a predefined time window (P1: LSF: 95-165; HSF: 135-205; N170: LSF: 170-270; HSF: 200-300) were used instead of peak amplitudes, because visual inspection indicated that emotional effects were present across a broader time range and did not occur at the peak only. Given the number of factors involved, hypothesis-driven analyses were carried out to provide sensitive tests of the a priori predictions for each SF type (Tabachnik & Fidell, 2001). Peak amplitude was pooled across the involved electrodes and subjected to a 2 (Emotion: neutral/fear) x 2 (Group: controls; ASD) ANOVA, separately for HSF and LSF to test the prediction that emotion processing would be driven by HSF in the ASD group and mediated by LSF in controls. Significant interactions were further tested using planned comparisons.

Results

Grating Task

P1 and N2 Amplitude and Latency

Grand Averages of the P1 and N2 are shown in figure 3. There was a significant interaction between SF and Group ($F(1, 37) = 8.82$, $p < .01$) for P1. Further analysis of this interaction indicated that in the ASD group HSF elicited significantly larger P1 compared to LSF ($t(16) = -2.17$, $p < .05$), whereas in controls the pattern was reversed: LSF gratings evoked larger amplitudes than HSF gratings ($t(21) = 2.18$, $p < .05$). Comparison of HSF between groups indicates that this was mainly due to enhanced activity to HSF in the ASD group ($t(37) = -1.88$, p

<.05, one-tailed). A similar pattern was found when only taking into account the participants that took part in the facial emotion task (SF x Group ($F(1, 29)= 7.24$, $p < .05$) . With respect to P1 latency, there was a main effect of SF, indicating faster latencies for LSF compared to HSF irrespective of group $F(1,37) = 27.77$, $p < .001$). For N2 a significant main effect of SF was found $F(1,37) = 35.72$, $p < .001$) with larger amplitudes for LSF compared to HSF in both groups.

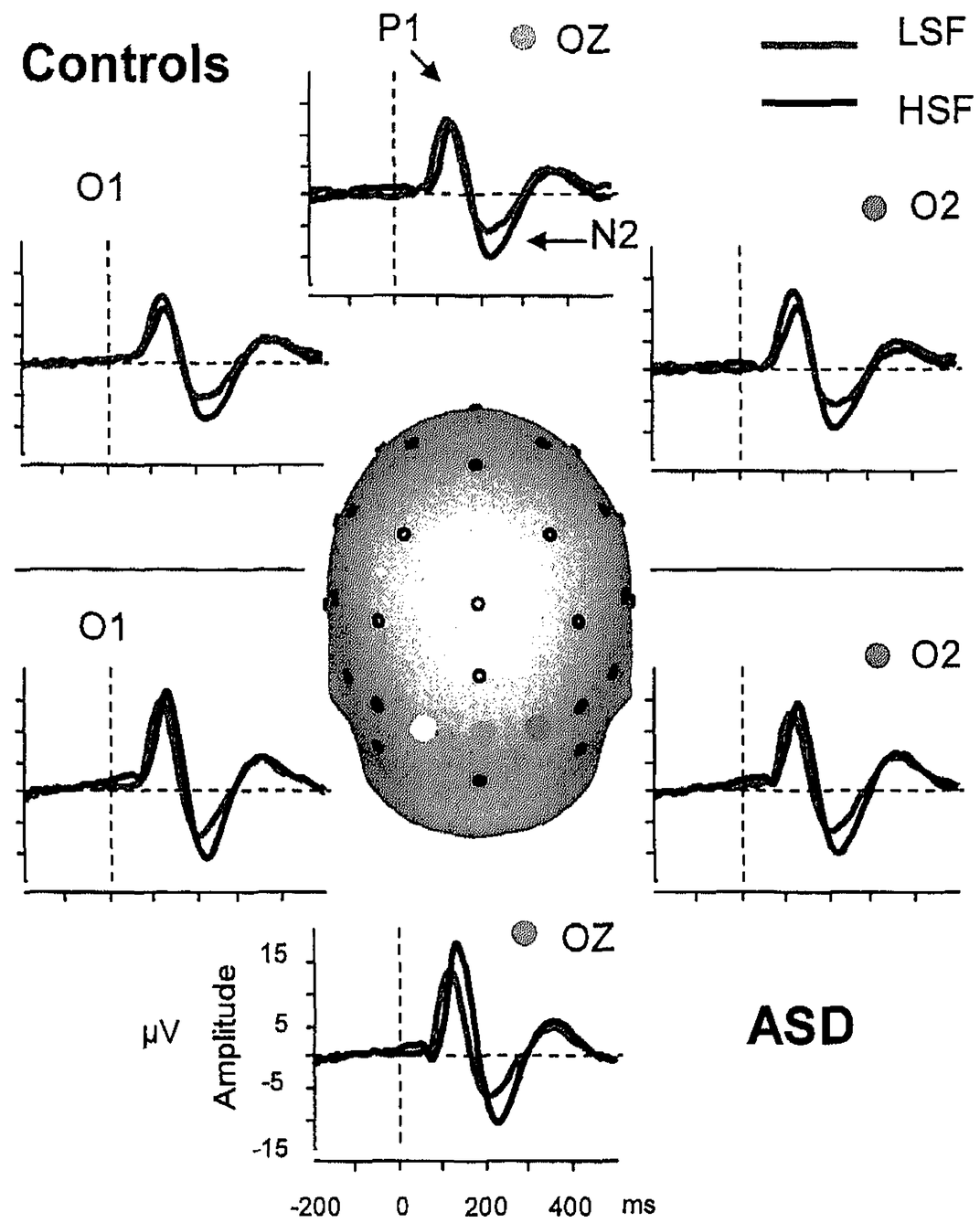

Figure 3. Grand-average VEPs at Oz, O1 and O2 in response to high (HSF) and low spatial frequency (LSF) gratings (in black and red, respectively) for both groups. Upper, control group; lower, ASD group.

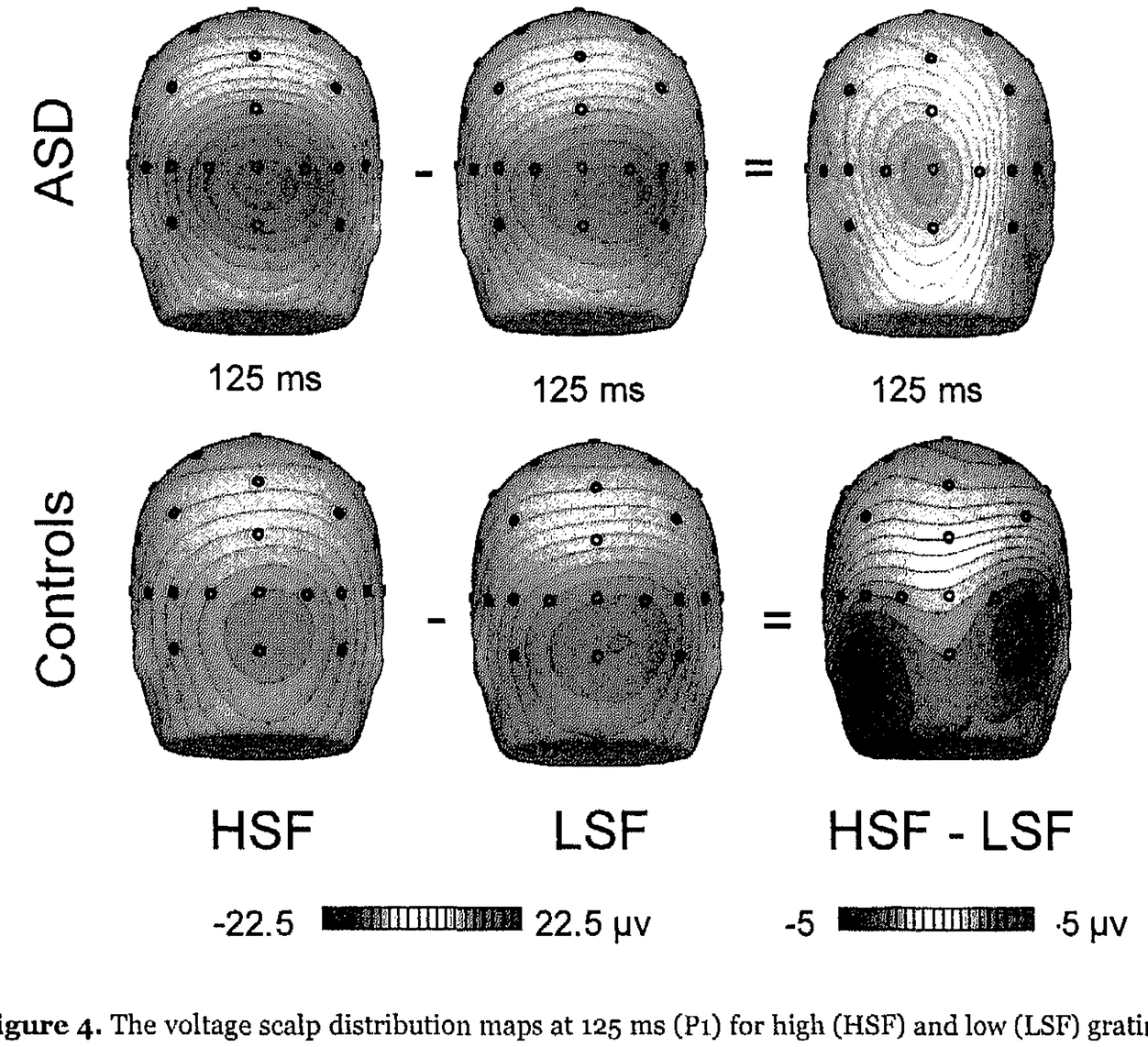

Figure 4. The voltage scalp distribution maps at 125 ms (P1) for high (HSF) and low (LSF) gratings for control children (lower) and children with ASD (upper). In addition, the voltage scalp distribution of the difference in ERP amplitude between HSF and LSF is shown (HSF-LSF) at 125 ms.

Facial Emotion task.

P1 and N170 Amplitude and Latency

Grand Averages of the P1 and N170 are shown in figure 5. As expected, a significant interaction between group and emotion was present for both HSF ($F(1,29) = 5.83$, $p < .05$) and LSF ($F(1,29) = 4.53$, $p < .05$) for P1. Importantly and consistent with the predictions, the emotion effect at P1 was only significant for HSF in the ASD group ($t(15) = 3.03$, $p < .01$) and for LSF in the controls ($t(14) = -2.23$, $p < .05$). In children with ASD fearful faces relative to neutral faces elicited enhanced activity in the HSF condition, whereas control children showed enhanced activity to neutral compared to fearful faces in the LSF condition (see figure 5). Children with ASD showed no emotion effect in the LSF condition ($t(14) = .84$, $p < .84$) and controls did not show an effect in the HSF condition ($t(15) = 1.37$, $p < .20$).
No significant effects were found for the N170.

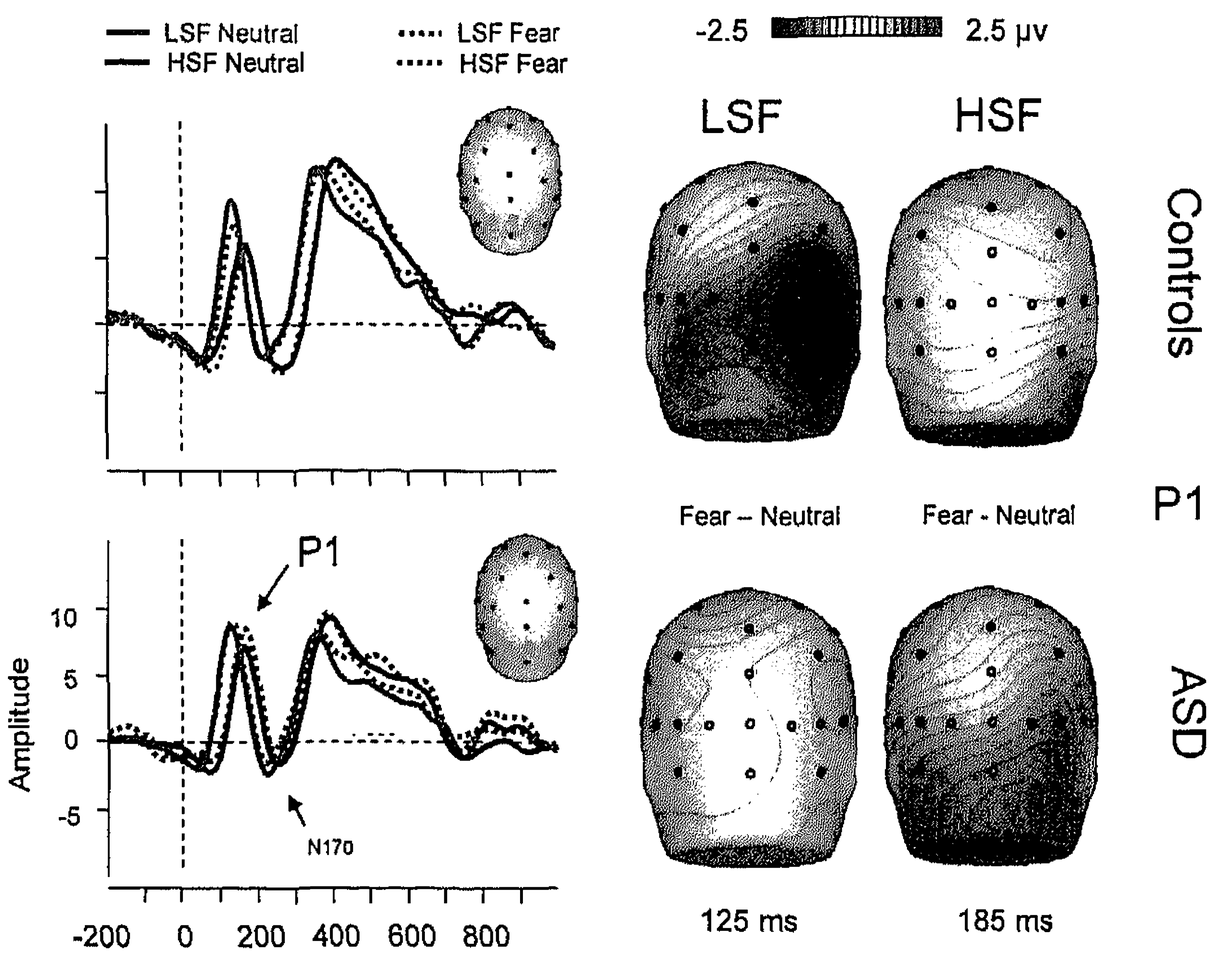

Figure 5. Grand-average ERPs at pooled electrodes PO7, PO8, Oz, O1 and O2 in response to HSF (black) and LSF (red) fearful (dashed) and neutral (continuous) faces for both groups. Upper, control group; lower, ASD group. In addition, the voltage scalp distribution of the difference in ERP amplitude between Fearful and Neutral expressions (Fear-Neutral) at the P1 peak (LSF: 125 ms; HSF: 185 ms) is shown for high (HSF) and low (LSF) spatial frequencies.

Discussion

Abnormalities in visual perception in ASD, in particular a more detailed oriented perception, are seen as primary or at least contributory to problems in face processing in ASD (see for review Dakin & Frith 2005; Happe & Frith, 2006; Mottron et al., 2006; Behrmann et al., 2006). However, there is little knowledge on the role of perceptual abnormalities in young children with ASD. In the present study we investigated a fundamental aspect of vision that is related to detail perception, spatial frequency processing, in young children with ASD using Visual Evoked Potentials to HSF (detailed) and LSF (global) patterns. Results show enhanced processing of HSF gratings in the early stages of visual processing (P1) in 3- and 4-year-olds with ASD compared to mental age matched controls. These effects relate well to previous studies that show enhanced processing of detailed information in ASD, including a recent study which found relative strengths in visuospatial disembedding and detail-focused processing in a non-verbal intelligence test in 3-4 year olds with ASD (Kuschner, Bennetto, & Yost, 2007).

Importantly, all children tested in the present study met strict criteria for an ASD disorder on both a parent interview and a child observation instrument and were well matched with controls on chronological and verbal age as well as levels of attention (by scoring and correcting for looking behavior). The group differences found with respect to HSF in the grating task cannot be caused by differences in acuity or contrast sensitivity between the groups. The SF range (6 c/d) of the gratings was well within the range of grating acuity at 3-4 years (Mayer & Dobson, 1982) and gratings were presented at maximal (100 %) contrast. Also, all individuals had normal or corrected to normal vision.

Remarkably, the increased P1 activity to HSF compared to LSF brain activity of children with ASD to gratings, resembles activity patterns seen in healthy adults. (Boeschoten et al., 2005; Plant, 1983; Reed, Marx, & May, 1984; Vassilev, Mihaylova, & Bonnet, 1983; Kenemans et al. 2000; Baas et al., 2002). In contrast, and consistent with the literature, our typically developing young children show relatively small amplitudes to HSF stimuli (Gordon & McCullouch, 1999). The latter effect has been suggested to reflect relatively late development of the system carrying high contrast and HSF information, the parvocellular system. In light of this literature, the present results might suggest that the parvocellular system is more developed in 3-4-year-olds with ASD. However, alternative explanations should also be considered, as VEPs are recorded from cortical neurons, which are not linked in a one-to-one manner with the parvo- and magnocellular system (Skottun & Skoyls, 2007). It is well possible that children with ASD have other abnormalities in visual cortical areas (e.g. neuronal tuning to a higher range of SFs), or show abnormalities in the macular part of the retina, which is also important for the processing of detailed information.

Importantly, the present study indicates that abnormalities in spatial frequency processing are not restricted to non-social (grating) stimuli, but are also reflected in early face processing in the same age group. We provide for the first time evidence that rapid effects of emotion (reflected in the P1 amplitude) are driven by HSF information in 3- and 4-year-olds with ASD, whereas in control children emotional effects are driven by LSF (see also Pourtois et al., 2005). In agreement with a previous study (Batty & Taylor, 2006), emotion did not yet influence the N170 in the present age group.

The lack of any effect of emotion in the LSF condition in ASD is in agreement with several suggestions that the rapid LSF 'quick and dirty' route involving the amygdala, for the processing of facial expressions, is dysfunctional in ASD (Laycock et al., 2007; Johnson; 2005 Deruelle et al., 2008). The present results are also in agreement with behavioral evidence in older children and adults showing that emotional effects are not absent in ASD but that the recognition of emotion and identity is primarily driven by HSF information (Deruelle et al., 2008; Curby et al., 2007; Deruelle et al., 2004). From a developmental point of view, early tuning towards HSF information in faces might directly affect the quality of

information obtained from a face in later life. The subcortical LSF face processing system has been suggested to lay the foundation for what later becomes the adult face processing network (Johnson, 2005). An early imbalance in the processing of spatial frequencies, as found in the present study, might affect the normal development of such a network.

Unexpectedly, the emotional effects found in controls reflected enhanced amplitudes to neutral compared to fearful faces. In adults typically enhanced amplitudes to emotional faces as compared to neutral faces are found. However, a study of Thomas et al. (2001) showed that whereas in adults the amygdala is more active to fearfull compared to neutral faces, in children the amygdala is most active to neutral faces, probably due to the fact that this stimulus category is ambiguous for children. As the amygdala is involved in the fast, LSF mediated route, this specific enhanced activation in not seen in the clinical group.

In sum, the present study provides the first evidence for a basic abnormality in visual processing, directly relevant for (the development of) face processing in a young age group of children with ASD. More specifically, children with ASD showed enhanced processing of HSF information, both for neutral stimuli (gratings) as well as for socially relevant information (emotional expressions). The lack of emotion effects in the LSF condition, might suggests that the rapid LSF route for facial expression processing is affected at an early stage in ASD.

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Is the early modulation of brain activity by fearful facial expressions primarily mediated by coarse low spatial frequency information in adults?

4

Vlamings, P. H. J. M., Goffaux, V., & Kemner, C.

Journal of Vision (in press).

Rapidly decoding the emotional content of a face is an important skill for successful social behavior. Several Event Related brain Potential (ERP) have indicated that emotional expressions already influence brain activity as early as 100 ms. Some studies hypothesized that this early brain response to fear depends on coarse-magnocellular input, which are primarily driven by Low Spatial Frequency (LSF) cues. Until now however, evidence is inconclusive probably due to the divergent methods used to match luminance and contrast across spatial frequencies and emotional stimuli. In the present study we measured ERPs to LSF and HSF faces with fearful or neutral expressions when contrast and luminance was matched across SF or not. Our findings clearly show that fearful facial expressions increases the amplitude of P1 (only for contrast-luminance equated images) and N170 in comparison to neutral faces but only in LSF faces, irrespective of contrast or luminance equalization, further suggesting that LSF information plays a crucial role in the early brain responses to fear. Furthermore we found that, irrespective of luminance or contrast equalization, the N170 occurred faster when perceiving LSF faces than HSF faces, again emphasizing the primacy of LSF processing in early face perception.

Chapter 4

Introduction

Rapidly decoding the emotional content of a face is an important skill for successful social behavior, since it helps to evaluate the states and intentions of others and to adapt future behavior. The time course of emotional face processing has been explored in several EEG and MEG studies. These studies report that particularly negative expressions affect the amplitude and/or latency of various early ERP and MEG components related to face processing. The two most prominently studied components are the P1 (e.g., Ashley, Vuilleumier & Swick, 2004; Batty & Taylor, 2003; Pizzagalli, Regard & Lehmann, 1999; Pizzagalli et al., 2002) and the N170 (e.g., Campanella, Quinet, Bruyer, Crommelinck & Guerit, 2002; Batty & Taylor, 2003; Righart & de Gelder, 2005; Stekelenburg & de Gelder, 2004). The P1 is a fast exogenous response to visual stimulation, which reflects striate as well as extrastriate visual processing (Heinze et al., 1994; Gomez, Clark, Luck, Fan & Hillyard, 1994; Rossion et al., 1999). It occurs about 100 ms after stimulus onset and is located over lateral occipital regions of the scalp. The N170 occurs at around 170 ms and is maximally recorded at occipito-temporal electrodes (Bentin, Allison, Puce, Perez & McCarthy, 1996). The N170 is the earliest ERP component to consistently show larger amplitude for faces than other non-face object categories (e.g. Jacques & Rossion, 2004). The N170 originates from a network of regions, probably including the fusiform gyrus, inferior occipital cortex, superior temporal sulcus and the inferior, middle and superior temporal gyri (Henson et al., 2003). The N170 reflects not only the detection of a face, but also the encoding of the structure or configuration of the face, based on which individual faces can be discriminated from each other (Jacques & Rossion, 2006).

A faster P1 for fearful expressions as compared to neutral expressions has been noted in several studies, and is consistent with the idea that negative emotions tend to capture attention in an involuntary reflexive manner and, as a consequence, tend to be processed faster (Williams et al., 2004; Pourtois, Grandjean, Sander & Vuilleumier, 2004; Pourtois, Dan, Grandjean, Sander & Vuilleumier, 2005; Lidell, Williams, Rathjen, Shevrin & Gordon, 2004; Eimer & Holmes, 2002). Other studies report effects of emotional expressions only somewhat later, at the level of the face-specific N170 (Blau, Maurer, Tottenham & McCandliss, 2007; Campanella et al., 2002; Batty & Taylor, 2003; Stekelenburg & de Gelder, 2004).

Overall, the above mentioned ERP studies underline the rapid processing of emotional expressions. However, facial expressions are complex stimuli and it is still not clear what information the visual system extracts in order to decode emotional expressions at such an early stage. Any input to the visual system consists of luminance variations occurring at various frequencies across space (e.g. Goldstein, 1999; de Valois & de Valois, 1988). Low spatial frequencies (LSF)

of an image capture large-scale luminance variations (i.e., coarse information) whereas high spatial frequencies (HSF) represent small-scale luminance variations of the image (i.e., fine information; Goldstein, 1999; de Valois & de Valois, 1988). The spatial frequency content of a stimulus is generally expressed in cycles per degree of visual angle (c/deg). The present experiment addresses the visual input properties of facial expression processing by means of spatial frequency filtering.

Two fMRI studies have now provided evidence for the importance of LSF information in emotional expression processing. One study showed that LSF information in a face is crucial to produce an increase in activation to fearful relative to neutral faces in the amygdala (Vuilleumier, Armony, Driver, & Dolan, 2003), a key subcortical structure in emotional processing (Morris, Ohman & Dolan, 1999; Whalen et al., 1998). In contrast, high spatial-frequency (HSF) information in faces did not evoke a differential response to fearful compared to neutral expressions in the amygdala. A similar pattern was found in the fusiform cortex. (Winston, Vuilleumier & Dolan, 2003; Vuilleumier et al., 2003; 2004). Given the modulatory role of the amygdala (Morris et al., 1998; Rotshtein, Malach, Hadar, Graif & Hendler, 2001), the hypothesis was raised that the enhanced processing of fear in the visual areas (including fusiform gyrus) is primarily mediated by rapid LSF cues, possibly via feedback from the amygdala which gets input from a rapid magnocellular tecto-pulvinar pathway, preferentially tuned to LSF (Pourtois et al., 2005; Winston et al., 2003; Vuilleumier et al., 2003). However, since fMRI has a low temporal resolution, the observed activation patterns may alternatively mirror SF differences occurring at late decisional stages rather than at the early visual analyses.

In contrast to fMRI, the technique of ERP has a high temporal resolution and is therefore well suited to give insight into the stages at which LSF and HSF input become important for facial expression processing in visual brain areas. However, only two ERP studies investigated the respective contribution of LSF and HSF to early facial expression processing (Holmes, Winston & Eimer, 2005; Pourtois et al., 2005). An increased P1 for LSF fearful expressions relative to LSF neutral expression was found at occipito-temporal electrodes by Pourtois et al., (2005). In the other study, by Holmes et al. (2005b), the occipito-temporal P1 was not analysed. At the level of the N170, neither study found an interaction between spatial frequency and emotional expression.

However, methodological aspects may account for the reported absence of SF influence on the early processing of facial expressions. A problem is that, when investigating SF processing, outputs of LSF and HSF filtering differ not only at the level of the spatial scale of information they convey, but also in terms of luminance and contrast. This is related to the fact that the frequency power in natural stimuli is maximal at low SF and almost exponentially decays at higher SF (see for review Loftus & Harley, 2005). In the study of Pourtois et al. (2005), the

overall difference in luminance and contrast between LSF and HSF images was matched by using hybrid stimuli. Pourtois et al. (2005) combined the LSF content of a given face (shown upright) with the HSF content of the same face presented upside-down, or vice versa. However, since contrast/luminance was not equated between LSF and HSF components within a given hybrid, superimposing an inverted LSF image on a HSF image may have disrupted perception of the expression carried by HSF more strongly, than superimposing an inverted HSF image on a LSF image (see Pourtois et al., 2005, figure 1). This might have prevented the detection of an effect of emotional expression at the level of the P1 and/or N170 for HSF faces.

The aim of the present study was to further explore the contribution of LSF and HSF to early emotional processing of faces, as reflected by P1 and N170 ERP components. To evaluate whether SF differences previously reported for emotion processing can be accounted by contrast and luminance, we directly investigated emotional processing when luminance and contrast were equated or not across LSF and HSF, within one study.

Differential sensitivity to HSF and LSF content of emotional expression is also apparent in some behavioral tasks. Whereas HSF seem to be relevant for the elaborate rating of emotional expressiveness as well as emotion discrimination (Schyns & Oliva, 1999; Vuilleumier et al., 2003; but see Goren & Wilson (2006) for different effects using synthetic faces), LSF are important for rapid attentional reponses to fear (Holmes, Green & Vuilleumier, 2005) as well as rapid categorization of happiness, sadness and anger (Schyns & Oliva, 1999), although the latter has not been investigated for fear. Complementing experiment 1, we will investigate in experiment 2 whether an LSF advantage for the processing of fear is reflected in reaction times (RT) when subjects have to rapidly categorize neutral and fearful faces. Because RT reflect the final stage of information processing, at which information about the facial expression of a face might be available in both LSF and HSF, RT may reveal emotion effects for HSF faces as well. We also evaluated whether differential effects in SF and emotion in RT are related to differences in luminance and contrast between the images.

Experiment 1

Methods

Participants

Twenty students (10 females and 10 males: mean age: 21.7 (SD = 2.7)) from Maastricht University participated in this study. Four participants were left-handed, the others were right-handed. All participants had normal or corrected-to-normal vision. The experiment was approved by the ethical committee and participants gave written informed consent before participation.

Stimuli

Face stimuli consisted of 16 grayscale images (8 males; 8 females), one half depicting a neutral expression, the other half depicting a fearful expression. Different identities displayed different emotions. The photographs were taken from the NimStim Face Set (http://www.macbrain.org/faces/index.htm, Tottenham, Borscheid, Ellertsen, Marcus & Nelson, 2002) and have shown to evoke emotional effects at the level of the N170 (Blau et al., 2007). Face images included European-American and African-American models. Face pictures were trimmed to remove external features (neck, ears and hairline). All pictures were fitted in a gray frame of 500 x 700 pixels. Each face subtended 6.3 degrees of visual angle (at a 113-cm viewing distance). The HSF images were created by filtering the original photographs, using a high-pass cut-off that was ≥ 6 cycles/deg of visual angle (≥ 36 cycles per object). The LSF images were created using a low-pass filter that was ≤ 2 cycles/deg of visual angle (≤ 12 cycles per object). These cut-off's (≤ 2 cycles/deg; ≥ 6 cycles/deg) were based on previous literature (e.g., Costen, Parker & Craw, 1994; Schyns and Oliva, 1999; Goffaux, Gauthier & Rossion, 2003; Deruelle, Rondan, Gepner & Tardif, 2004; Boeschoten, Kenemans, Kemner & van Engeland, 2007; Deruelle and Fagot, 2005; Deruelle, Rondan, Salle-Collemiche, Bastard-Rosset & Da Fonséca, 2008). Filtering was performed in Matlab (The Mathworks, Natick, MA) using a set of Gaussian filters. After the filtering, HSF and LSF stimuli largely differed in terms of luminance and Root Mean Square (RMS) contrast (LSF: Mean luminance: 147; RMS contrast: 40; HSF: Mean Luminance: 131; RMS Contrast: 12.5). RMS contrast has been shown to be the best index for perceived contrast in natural images (Bex and Makous, 2002). Finally, global contrast and luminance were equated across scales by assigning both HSF and LSF images the mean luminance and RMS contrast of the 16 original broadband photographs (Mean Luminance: 141; RMS contrast:

29), see figure 1. Since original contrast and luminance of LSF filtered faces were naturally close to full spectrum values, the equalization of these parameters to full spectrum values mostly affected HSF faces.

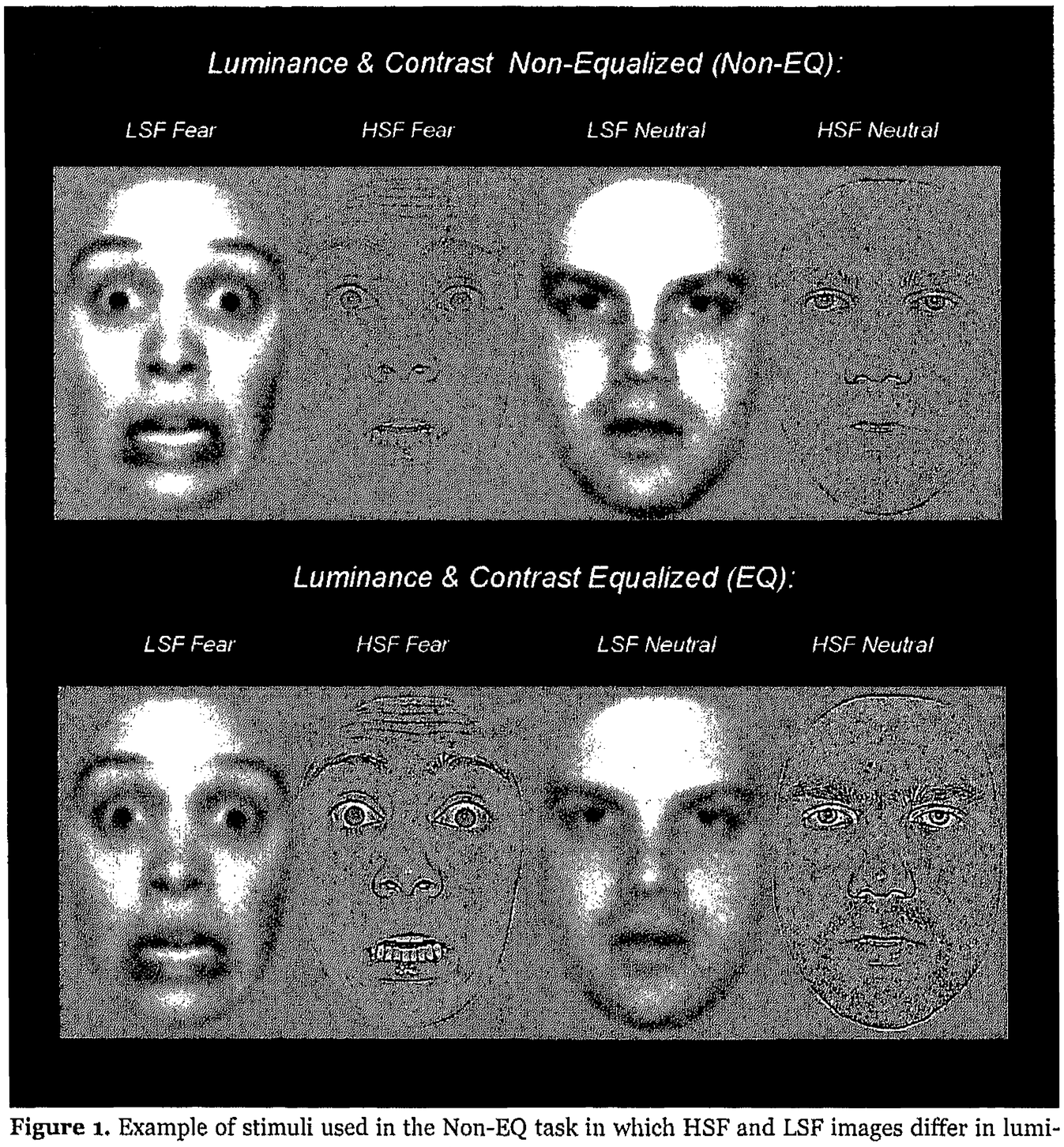

Figure 1. Example of stimuli used in the Non-EQ task in which HSF and LSF images differ in luminance and contrast, and the EQ task in which HSF and LSF stimuli were matched on contrast and luminance.

Procedure

Participants were seated in a dimly and quiet room and were presented with two series (in a counterbalanced order) of 4 experimental blocks of 79 trials each. In one series HSF and LSF faces were equated for luminance and contrast, in the other series luminance and contrast differed between HSF and LSF images. Each block contained 32 neutral face trials (HSF and LSF) and 32 fearful face

trials (HSF and LSF), each presented for 500 ms, in randomized order with an interstimulus interval that varied randomly between 1600-1800 ms. To maintain attention to the task, each block contained 15 animation figures (for example Disney figures), each with a duration of 2 seconds. Participants had to press a response button as soon as they saw an animation figure on the screen and had to refrain from responding to all other images. Animation figures were included because we want to conduct this experiment with children in the future.

ERP recording and data-analysis

During task performance the EEG (0.1- 200 Hz, sampling rate 500 Hz) was recorded with a 31-channel Quickcap (Neuromedical supplies of Neurosoft Inc.) covering frontal, central, temporal and parietal scalp areas. An electrode attached at the left mastoid served as a reference. Afz was used as ground electrode. Blink and vertical eye movements were monitored with electrodes placed at the sub- and supra-orbital ridge of the right eye. Lateral eye movements were monitored with two electrodes placed on the right and left external canthi. All electrode impedances (EEG and EOG) were kept below 10kOhm.

The EEG data was analyzed off-line using 'Vision Analyser' software (Brain Products, Munich, Germany). A common average reference was recomputed for all electrodes. EEG epochs were extracted beginning 200 ms before and ending 400 ms after each stimulus. The 200 ms prior to stimulus onset was used as baseline. The epochs were bandpass filtered with a 30Hz, 24 dB/octave low pass filter. Artefacts from vertical eye movements and blinks were reduced with the algorithm of Gratton et al. (1983). Thereafter all epochs containing artefacts, amplitudes larger than 75 μV, were removed. Separate ERP averages were computed for the four stimulus conditions (SF (HSF/LSF) x Emotion (Fear/Neutral). For each condition, P1 and N170 latencies and amplitudes were automatically extracted at peak-maximum occipito-temporal electrodes PO7/PO8 and P7/P8 (time windows: P1: 70-140 ms; N170: 100-200 ms). Both P1 and N170 were largest at these electrodes. All peaks were confirmed by visual inspection. Latency and amplitude values were subjected to a repeated-measure ANOVA with SF (HSF versus LSF), Emotion (Fear versus Neutral), Equalization (luminance/contrast equalised, i.e., EQ versus luminance/contrast non-equalised, i.e., Non-EQ), Electrode Position (posterior versus posterior-occipital) and Hemisphere (Left versus Right) as within-subject factors. Based on a priori hypothesis conditions were further compared using paired t-tests.

Chapter 4

Results

Figure 2 shows the grand averages for neutral and fearful HSF and LSF faces at PO7/PO8 and P7/P8, separately for EQ and Non-EQ stimuli.

P1 Amplitude

Statistical analysis of P1 amplitudes revealed a significant interaction between SF, Emotion, Equalization and Hemisphere ($F(1,19) = 7.62$, $p < .05$). Separate analysis for left and right hemisphere showed that the SF x Emotion x Equalization interaction was only significant for the right hemisphere ($F(1,19) = 6.22$, $p < .05$). Further analysis indicated that there was a significant interaction between Emotion and Equalization at P8/PO8 solely in LSF ($F(1,19(= 4.56$, $p < .05$). Hence, pairwise comparisons computed on P8/PO8 electrodes showed that LSF fearful faces elicited larger P1 amplitudes than LSF neutral faces only in EQ condition ($t(19) = -2.39$, $p < .05$).

P1 Latency

The overall four-way ANOVA indicated a significant interaction between SF and Emotion ($F(1,19) = 5.65$, $p < .05$). Further analysis of this interaction indicated that faster latencies for LSF vs. HSF faces occurred irrespective of facial expression (neutral: $t(19) = 5.48$, $p < .001$; fear: $t(19) = 5.24$, $p < .001$). Yet, there was a trend toward a significant effect of emotion for LSF faces only ($t(19) = -1.788$, $p = .090$). SF x Equalization interaction was also significant ($F(1,19) = 8.15$, $p < .05$) indicating significantly longer latencies for HSF non-EQ faces compared to HSF EQ faces ($t(19) = -2.45$, $p = <.05$) whereas in the LSF condition, there was no latency difference between EQ and non-EQ conditions. In addition, faster latencies for LSF vs. HSF faces were found for both EQ (mean difference: 6 ms; $t(19) = 4.11$, $p = .001$) and non-EQ faces (mean difference 13 ms; $t(19) = 5.11$, $p = <.001$).

N170 Amplitude

Statistical analysis of N170 amplitude indicated a significant main effect of Hemisphere ($F(1,19) = 7.46$, $p < .05$). Larger N170 amplitudes were found for the

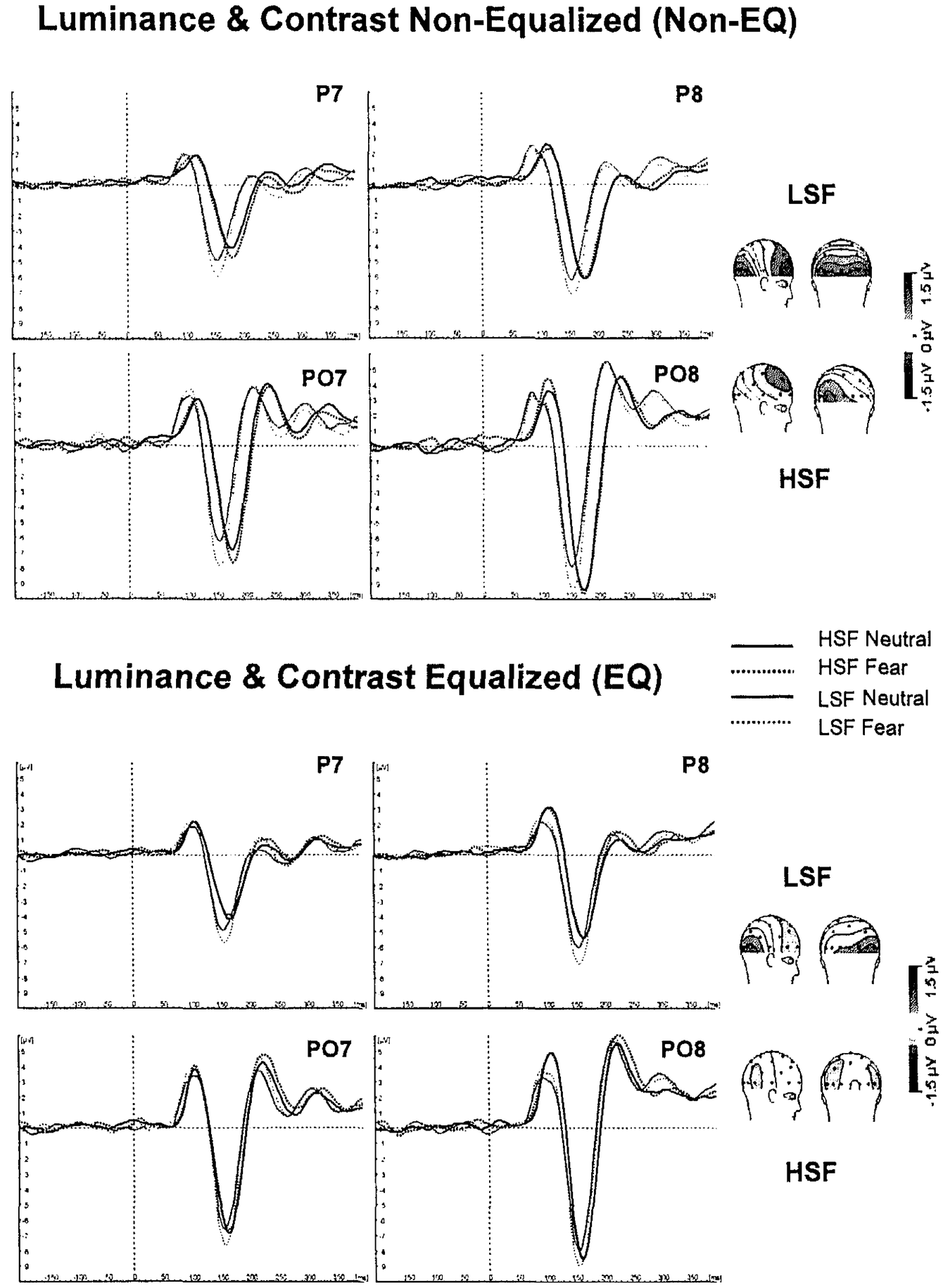

Figure 2. Grand averages for HSF (black) and LSF (gray) fearful (dashed) and neutral (continuous) faces at channel P7/P8 and PO7/PO8. Fearful faces elicit larger amplitudes than neutral faces in the LSF condition only. Furthermore the topographical distribution of the difference (Neutral minus Fear (160-220 ms)) in ERP activity between fearful and neutral faces is shown for the N170. Note that the difference covers the ventro-temporal areas.

right compared to the left hemisphere. Furthermore there was a significant interaction between SF, Emotion and Electrode ($F(1,19) = 4.99$, $p < .05$). ANOVA separately conducted in LSF and HSF indicated a significant interaction between Emotion and Electrode for LSF faces only ($F(1,19) = 22.09$, $p < .01$). Although LSF fearful faces elicited larger N170 amplitudes compared to neutral faces at both electrode positions (PO7/PO8: $t(19) = 8.23$, $p < .001$, P7/P8: $t(19) = 9.17$, $p < .001$), this effect was stronger on PO7/PO8 (mean difference: 1.43 μV) as compared to P7/P8 electrodes (mean difference: 1.03 μV).

N170 Latency

The overall four-way ANOVA indicated a significant SF x Equalization interaction ($F(1,19) = 82.52$, $p < .001$). Further analysis of this interaction indicated a significant effect of SF in both EQ and non-EQ conditions (Non-EQ: $F(1,19) = 12.07$, $p < .001$; EQ: $F(1,19) = 7.31$, $p < .001$) with shorter latencies for LSF compared to HSF faces. Yet, N170 latency differences between HSF and LSF were larger in non EQ (mean difference: 23 ms) than EQ conditions (mean difference: 8 ms). Furthermore, HSF faces in the Non-EQ task, showed significantly longer latencies than HSF faces in the Non-EQ task ($t(19) = -4.93$, $p < .001$) whereas there was no difference between EQ and non-EQ images for LSF faces.

Summary

Consistent with our hypotheses, the early influences of emotion as observed at the level of P1 and N170 amplitude were only present in the LSF condition. For the P1, the effect of emotion in the LSF condition was only significant in right hemisphere and only in the equalized condition. In contrast, for the N170 this effect was found irrespective of contrast equalization. In addition a main effect of SF was found for P1 and N170 latency, indicating faster latencies for LSF compared to HSF faces. This effect was found irrespective of contrast equalization, although it was smaller in the equalized condition due faster latencies to HSF images.

Experiment 2

In this experiment we investigated whether the LSF advantage for the processing of facial expressions found in ERPs in experiment 1, using a passive paradigm, is also reflected in reaction times when subjects have to perform an active categorization task on emotional expression. Although an LSF bias has been shown for

The role of HSF and LSF information in facial expression processing in adults

the rapid categorization of emotional stimuli including happiness, sadness and anger (Schyns & Oliva, 1999), this has not been investigated for fear. There is however evidence that LSF are important for rapid attentional responses to fear (Holmes et al., 2005a). Based on our ERP findings and literature we predict increased sensitivity to fear in LSF, and faster categorization of LSF fearful compared to LSF neutral faces. Alternatively, in contrast to ERP observations, emotion effects on RT may be obvious on both scales. Contrary to P1 and N170, behavioral RT reflects the final stage of visual processing. At this final stage information about the facial expression of a face might be available in both LSF and HSF and RT may reveal emotion effects for HSF faces as well.

Participants

Twenty adult subjects (10 women and 10 men; mean age: 22.21 years (SD: 2.97)) participated in this experiment. The data of one participant were not included in the analysis because performance was below chance in one of the conditions. One participant was left-handed, the others were right handed. Participant had normal or corrected to normal vision.

Stimuli, task and data-analysis

Experimental conditions were identical to experiment 1 (same stimuli, same duration etc.), except that no animation figures occurred between face stimuli and that participants had to decide whether the presented stimulus was a fearful or a neutral face by pressing the appropriate keyboard button (left/right arrow). Key assignments were counterbalanced across subjects. Instructions emphasized speeded and accurate decisions. Trials with reaction times shorter than 150 ms and expanding 1500 ms were discarded. Reaction times were subjected to a SF (HSF/LSF) x Emotion (Neutral/Fear) x Equalization (Non-EQ/EQ) repeated-measure ANOVA. Furthermore bias-free sensitivity indexes (d') were computed for each subject in all conditions (following Stanislaw & Todorov, 1999).

Results

Reaction times

Repeated-measures ANOVA revealed a main effect of emotion ($F(1,18) = 21.51$, $p < .001$) on RTs indicating shorter reaction times to fearful (mean: 544 ms) than neutral faces (mean: 566 ms; see Table 1). Furthermore a significant Spatial Frequency x Equalization interaction was found ($F(1,18) = 4.96$, $p < .05$). Further analysis of this interaction indicated that participants were overall faster at cate-

gorising LSF faces than HSF faces in both non-EQ (F (1,18) = 50.09, p < .001) and EQ conditions (F(1,18) = 15.28, p <.001) but that this effect was stronger in the Non-EQ task (see Table 1).

D'

SF significantly influenced d' (F(1,18) = 5.83, p < .05), indicating that participants were more sensitive to fear in the LSF condition than in the HSF condition, irrespective of equalization (see figure 3). There were no other significant effects or interactions on d'.

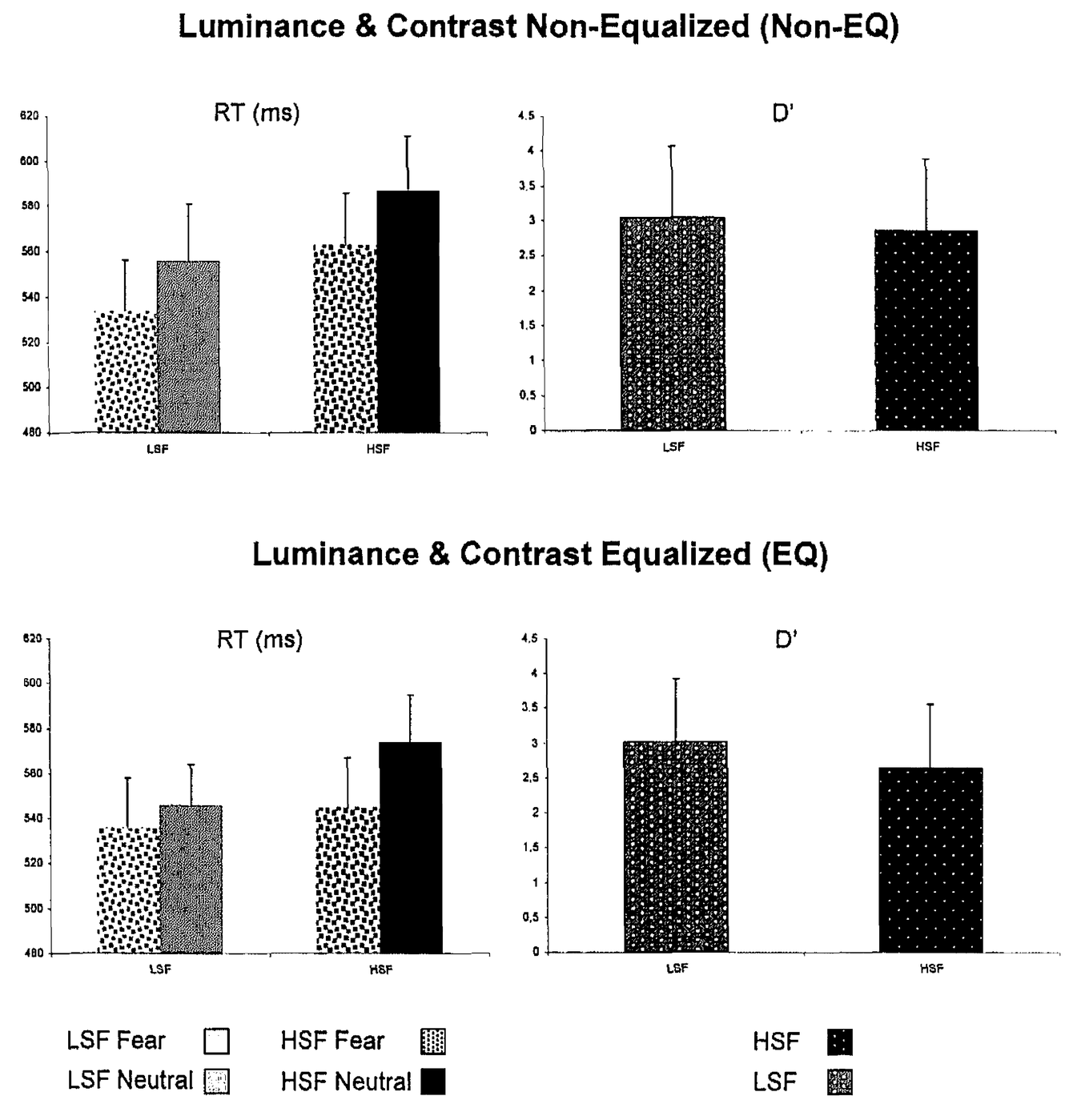

Figure 3. Mean reaction times (RT) and D' (+ SE) for all stimulus conditions in the Non-Equalised (Non-EQ) and Equalised (EQ) task.

Discussion

In the present study we investigated the role and time course of LSF and HSF information in the decoding of facial expressions. Based previous literature we expected to find that an early modulation of the P1 and/or N170 by facial expression is primarily mediated by LSF. The second goal of our study was to investigate whether SF influences on emotional processing genuinely reflect the differential involvement of LSF and HSF or whether these are merely due to contrast and luminance differences across SF. We used emotional stimuli that were known to affect ERPs in broadband viewing conditions (REF), and filtered them to preserve either HSF or LSF. HSF and LSF faces were either matched (i.e., EQ condition) or not matched (i.e., non-EQ condition) on luminance and contrast. As expected, emotional expression modulated the amplitude of early visual ERPs, but only when presented in LSF. The increased P1 amplitude for LSF fear was observed in the right hemisphere, and only when contrast/luminance was adjusted to fit full spectrum values (i.e., EQ condition). The N170 amplification related to LSF fear was observed in both EQ and non-EQ conditions. In contrast, HSF fear did not affect P1, or N170 amplitude.

Several studies have reported increased P1 amplitude for negative emotional compared to neutral broadband face stimuli (Pizzagalli et al., 1999; 2002; Batty & Taylor, 2003). Increased P1 amplitude may reflect the allocation of attentional resources to emotionally significant stimuli (Williams et al., 2004; Pourtois et al., 2004; 2005; Lidell et al, 2004; Eimer & Holmes, 2002). The present findings indicate that P1 modulation by facial expression is primarily driven by LSF cues. This effect was only significant in the right hemisphere, which is consistent with several studies that show a right hemisphere advantage for the processing of faces and emotional expressions (e.g. Rossion, Joyce, Corell & Tarr, 2003; Halgren, Raij, Marinkovic, Jousmaki & Hari, 2000; Kawasaki et al., 2001; Pizzagalli et al., 1999, 2002; Streit, Wöwler, Brinkmeyer, Ihl & Gaebel, 2000; Williams, Palmers, Lidell, Song & Gordon, 2006).

The present P1 findings are also in agreement with the study of Pourtois et al. (2005). These authors also showed that the early modulation of the P1 by facial expression was primarily driven by LSF. These authors controlled for luminance and contrast differences across scales by using hybrid stimuli. Hybrid stimuli are built by superimposing an LSF-filtered image with an image filtered to preserve HSF. However, in the study of Pourtois et al. (2005), contrast/luminance was not equated between LSF and HSF *within* a given hybrid. In the present study no hybrid stimuli were used and since the contribution of luminance and contrast was systematically addressed, we provide unequivocal evidence that P1 effects are primarily driven by LSF, using HSF and LSF stimuli that are matched on contrast and luminance. Emotion effects were absent for both HSF and LSF stimuli in the non equalised condition, possibly because early

visual evoked potentials are very sensitive to luminance and contrast alternations (Blau et al., 2007; Ellemberg, Hammarrenger, Lepore, Roy & Guillemot, 2001). Contrast and luminance differences across HSF and LSF trials in non equalised blocks might have impeded early P1 differences related to LSF emotion.

A recent ERP study found evidence for enhanced early brain responses in extrastriate areas to threatfull non-facial stimuli presented in LSF at occipital electrodes at a similar time range as the P1 (Carretié, Hinojosa, López-Martín & Tapia, 2007). This suggests that the early response to emotion in visual areas in the time range of the P1 is not face specific but possibly results from threat signals in general, irrespective of the object category, as was also suggested by Pourtois et al. (2005).

In addition to the findings on the P1, we also found an enhanced N170 to fearful expressions in LSF only. In contrast, Pourtois et al. (2005) and Holmes et al. (2005b) did not report any effect of emotion or interaction between emotion and SF for N170 amplitude. However, Pourtois et al. (2005) and Holmes et al. (2005b) also did not report emotion effects on the N170 in broadband viewing conditions in contrast to previous literature (Blau et al., 2007; Campanella et al., 2002; Batty & Taylor, 2003; Stekelenburg & de Gelder, 2004; Kromboltz, Schaefer & Boucsein, 2007; Eger, Jedynak, Iwaki & Skrandies, 2003). The N170 is thought to be a face specific component which reflects encoding of the structure of a face in such a way that it can be differentiated from others (Jacques & Rossion, 2006) and is influenced by emotional expressions (Blau et al., 2007; Campanella et al., 2002; Batty & Taylor, 2003; Stekelenburg & de Gelder, 2004). An absence of emotional processing at the N170 could be related to the mixed presentation of face stimuli (66%) and objects (33%) of similar size and color in the study of Holmes et al. (2005b) and the type of task (gender discrimination) in the study of Pourtois et al. (2005), which might take attention away from the emotional signals. To our knowledge, all previous studies using broadband stimuli also failed to report any N170 emotional effects when they used a mixed presentation of objects and face stimuli (Holmes, Vuilleumier, & Eimer, 2003; Ashley et al., 2004). Furthermore, Krombholz, Schaefer and Boucsein (2007) report that tasks in which facial emotion is irrelevant might impede emotional processing at the level of the N170. However, these suggestions are subject for future study and are beyond the scope of the present study. Nonetheless, the present results on the N170 show that early (< 170 ms) encoding of fearful facial expressions is based on LSF input. Importantly, the interaction between SF and Emotion was significant for both contrast/luminance EQ and Non-EQ images, indicating that the absence of an effect of emotion at the N170 is not merely due to HSF images being less luminant and containing less contrast than HSF images.

Schyns, Petro and Smith (2007) have provided interesting insights in how the N170 reflects face processing over time. More specifically, subjects categorized stimuli consisting of samples of information, randomly sampled in x, y and

SF dimensions of face images (see Figure 1, Schyns et al., 2007). On each trial a face was presented, that was partly revealed by a mid-grey mask punctured by a number of randomly located Gaussian windows (called 'bubbles') revealing information from five non-overlapping SF bands. By using classification image techniques, Schyns et al. (2007) investigated which combination of SF bands and image features was diagnostic for the categorization of each expression and how this related to the N170. Interestingly, the ERP results of Schyns et al. (2007) showed that the initial processing of a fearful face starts by processing of the eyes at around 120 ms post stimulus onset, and is followed by the processing of mouth information. Their data further suggest that LSF information located around the mouth and HSF information located around the eyes may be particularly diagnostic for processing facial fear (see figure 2 of Schyns et al., 2007); nevertheless, the authors did not explicitly address or quantify the HSF or LSF contribution to facial expression categorization.

In contrast to the study of Schyns et al. (2007), the contribution of the various facial features to the perception of fear cannot be disentangled in the present study, as only SF content was manipulated. However, it has been shown that facial expression processing as well as many other aspects of face processing, is not the mere outcome of purely local feature analyses but rather relies on the integration of features into a so-called holistic representation (Calder, Young, Keane, & Dean, 2000; Maurer, Le Grand, & Mondloch, 2002; see also for review Goffaux & Rossion, 2006). Since it decomposes face stimuli into parts, the use of bubbles may artificially induce a local bias in face emotional processing (Goffaux & Rossion, 2006; Rossion, 2008). In agreement with this suggestion, is the larger N170 amplitude in left hemisphere as well as the faster information integration, as reflected by shorter N170 peak in this hemisphere in the study of Schyns et al. (2007). Left hemisphere advantages for face processing (and other types of stimuli) have namely been specifically linked to local, as opposed to, global processing, which has been found to be dominated by the right hemisphere (see Iidaka, Yamashita, Kashikura & Yonekura, 2004).

In our ERP study, SF not only affected P1 and N170 amplitudes but also largely modulated their latencies. LSF images were processed faster than HSF images irrespective of luminance or contrast equalisation, as indicated by the shorter P1 and N170 latencies for LSF as compared to HSF images. Contrast/luminance equalization in the present study only influenced the processing of HSF faces, irrespective of emotional content. HSF images were more luminant and more contrasted in the EQ task than in the Non-EQ task. In contrast, luminance and contrast manipulation only slightly modulated LSF images across studies since their luminance/contrast was naturally close to broadband values to which they were normalized. Consequently, HSF EQ faces were processed faster than HSF non-EQ faces, as indicated by faster RT as well as shorter P1 and

N170 latencies. The higher contrast transmitted in HSF EQ images also induced larger P1 amplitudes.

SF influences on ERP latency are consistent with electrophysiological face studies that reported shorter ERP latencies to LSF than HSF facial stimuli (Halit, de Haan, Schyns & Johnson, 2006; Hsiao, Hsieh, Lin & Chan, 2005; McCarthy, Puce, Belger & Allision, 1999) as well as visual evoked potential studies that reported SF effects on ERP latency for non-facial stimuli (Mihaylova, Stomonyakov & Vassilev, 1999; Musselwhite & Jeffreys, 1985). This temporal precedence of LSF compared to HSF is consistent with previous findings that the neuronal pathways sensitive to LSF and HSF have dissociable time scales with faster cortical arrivals of information processed in the parvocellular (mainly sensitive to HSF) compared to magnocellular (mainly sensitive to LSF) system (Maunsell et al., 1999; Schroeder, Tenke, Arezzo & Vaughan, 1989; Bullier, Schall & Morel, 1996; Klistorner, Crewther & Crewther, 1997; see for review Laycock, Crewther & Crewther, 2007).

In experiment 2, we investigated whether the LSF advantage for the processing of facial expressions found in ERPs in experiment 1, would be reflected in RT when subjects have to complete an active categorization task. In contrast to the ERP findings, we found an effect of facial expression for both HSF and LSF faces in the EQ as well as the Non-EQ task. Participants decided more quickly that a face was fearful than that it was neutral, irrespective of SF content. RTs to HSF stimuli were overall slower than to LSF stimuli. This is consistent with several studies that indicate that stimuli signalling threat receive preferential attention over neutral stimuli, (see for review Holmes et al. 2005a) and behavioural studies indicating faster processing of LSF over HSF stimuli (Coin, Versace, & Tiberghien, 1992, Parker, Lishman & Hughes, 1992; 1997). The lack of interaction between SF and emotion in RT, could be related to the fact that RT reflects the final stage of information processing, when the facial expression of a face is available for both LSF and HSF. Our results suggest that HSF participate to fear processing but at a later stage (>170 ms). In addition to these reaction time effects and consistent with our ERP findings, analysis of SDT measures showed that subjects were more sensitive to fear in LSF faces than HSF faces, irrespective of contrast/luminance equalisation. This matches a recent study showing that a connectionist model better classified fearful faces based on LSF than HSF input (Mermillod, Guyader, Vuilleumier, Alleysson & Marendaz, 2005).

As a final point, we would like to discuss some limitations to the present study. It specifically aimed at investigating the role of HSF and LSF in facial expression processing. Like previous studies, the present study did not include intermediate SF bands, which are known to best carry face identity (Costen et al., 1994; Costen, Parker & Craw, 1996; Parker & Costen, 1999) and could also play a role in the rapid processing of facial expressions. To our knowledge, the role of intermediate SF to facial expression processing had not been studied and should

be addressed by measuring behavioural and electrophysiological responses to fear while SF content of face images is parametrically shifted from low to high spatial frequencies (see Tanskanen et al., 2005 for a similar approach using non-emotional faces).

Based on the observation that amygdala activity to fearful faces is related to the processing of LSF information, Vuilleumier et al. (2003) argued that amygdala has a rapid access to LSF components of visual information, either through a direct subcortical tecto-pulvinar route preferentially tuned to LSF information, or through the initial feedforward sweep within the visual system. Here, we provide high-temporal resolution evidence that LSF input is processed fast and drives the early detection of fearful expressions as indicated by an enhanced P1 and N170 across ventro-temporal areas for LSF only. Since the amygdala modulates activity in visual areas via feedback signals (Morris et al., 1998; Rotshtein et al., 2001), the amygdala may rapidly enhance ventral temporal visual responses to faces at the P1 and N170 latency. This hypothesis needs further investigations, combining EEG and fMRI methodology and connectivity analyses.

In sum, our behavioural as well psychophysiological findings indicate that LSF are important for the rapid extraction of facial expression information. For the first time we have shown that a modulation of the face specific N170 by facial expression is primarily mediated by LSF information and that this effect cannot be explained by differences in luminance and contrast between HSF and LSF faces. Furthermore, in a behavioural study we found that in addition to LSF, HSF also contain important information about the facial expression of a face, which might be important at a later stage of information processing. The present ERP findings might be important for all studies investigating the role of SF in facial expression recognition. Especially, for children with psychiatric disorders like autism, for whom deficits in LSF processing have been suggested (Johnson, 2005). For these populations the passive ERP technique, as used in the current study, is an excellent method.

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Reduced error monitoring in children with autism spectrum disorder: an ERP Study

5

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This study investigated self monitoring in children with Autism Spectrum Disorder (ASD) with Event Related Potentials looking at both the error related negativity (ERN) and error-related positivity (Pe). The ERN is related to early error/conflict detection and the Pe has been associated with conscious error evaluation or attention allocation. In addition, post-error slowing in reaction times was measured. Children with ASD and age and IQ matched controls were administered an easy and a hard version of an auditory decision task. Results showed that the ERN was smaller in children with ASD but localized in the Anterior Cingulate Cortex (ACC) in both groups. In addition we found a negativity on correct trials (CRN) which did not differ between the groups. Furthermore, a reduced Pe and a lack of post-error slowing in reaction times were found in children with ASD. The reduced ERN in children with ASD, in the presence of an intact CRN, might suggest a specific insensitivity to detect situations in which the chance of making errors is enhanced. This might in turn lead to reduced error awareness/ attention allocation to the erroneous event (reduced Pe) and eventually in a failure in change of strategy to deal with a situation, as becomes evident from the lack of post-error slowing in the ASD group. This relates well to the perseverative behaviour that is seen in children with ASD. We discuss these results in terms of a general deficit in self monitoring, underlying social disturbance in ASD and the involvement of the ACC.

Chapter 5

Introduction

Autism Spectrum Disorder (ASD) is a severe developmental disorder, characterized by impairments in social interaction and communication, and restricted behaviour and interests (American Psychiatric Association, 1994). The relation between specific brain abnormalities and atypical behaviour in ASD is still unclear. Recently, Allman, Watson, Tetreault and Hakeem (2005) found abnormal concentrations of spindle neurons in subjects with autism. Spindle neurons are large, bipolar cells located in layer 5 of anterior cingulate cortex (ACC) and frontoinsular cortex. It is hypothesized that spindle cells play a crucial role in the integration of reward and punishment probabilities (Allman et al., 2005), which is important in the ability to monitor and self-correct one's own thoughts and actions. Some studies have indeed shown a relation between ACC activity and adaptive behavior, especially the ability for self monitoring (Amiez, Joseph & Procyk , 2006; Hajcak, McDonald, & Simons, 2003). Several behavioural features in autism, like perseverative responding and an inability to adapt in social situations may reflect impaired self monitoring, which could be related to abnormal functioning of the ACC (Hill, 2004; Mundy, 2003; Russell, 1997; Henderson et al., 2006).

Indeed, decreased metabolism of the ACC has been reported in subjects with ASD (Haznedar, Buchsbaum, Metzger, Solimando, Spiegel-Cohen & Hollander, 1997; Haznedar et al., 2000). Furthermore children with ASD have difficulties in error correction and avoidance, which is suggestive of impaired self-monitoring (Rusell & Jarrold, 1998), although a monitoring deficit was not found in a second study (Rusell & Hill, 2001). However, so far there have been no studies in which ACC functioning was directly measured during self monitoring behavior in children with ASD.

Prominent in research on self-monitoring and ACC functioning are Event Related brain Potential (ERP) studies on self monitoring. Self monitoring is reflected in the so called error-related negativity (ERN) and error-related positivity (Pe) which occurs after an error has been made. In adults, the ERN peaks 50-100 ms after an erroneous response. Although the function of the ERN is still under debate, current theories interpret the ERN as reflecting the detection of post response conflict or mismatch between the actual (erroneous) response and the competing correct response tendency (Yeung, Cohen & Botvinick, 2004; Coles, Scheffers & Holroyd, 2001; Ullsperger & von Cramon, 2006). Recently the ERN has been ascribed a more general evaluative function, reflecting the outcome of a broad action-regulation system signaling expectancy violations (see for review Wiersma, van der Meere, and Roeyers, 2007). The Pe has a centroparietal distribution and follows the ERN around 200-500 msec after response and has been related to error awareness and the adjustment of response strategies, such as post error-slowing in reaction times (e.g. Falkenstein, Hoormann, Christ &

Hohnsbein, 2000; Hajcak, McDonald & Simons, 2003; Leuthold & Sommer, 1999). Dipole localization analyses (Luu, Flaisch & Tucker, 2000; Hermann, Römmler, Ehlis, Hedrich & Fallgater, 2004; van Veen & Carter, 2002; O'Connell et al., 2007), as well as functional MRI (fMRI) (e.g. Carter, Braver, Barch, Botvinick, Noll, & Cohen, 1998; Ullsperger & von Cramon, 2001) and MEG studies (Miltner, Lemke, Weiss, Holroyd, Scheffers & Coles, 2003) have convincingly associated both ERN and Pe activity with ACC functioning.

In the present study we aim to directly relate ACC functioning in children with ASD, as reflected in specific ERP peaks, to abnormal self monitoring. Based on the literature, which describes indications for ACC dysfunction as well as deficits in self-monitoring in ASD, we expect behavioral impairments in error processing as well as abnormalities in the ERN and Pe. Given the large individual differences in social symptoms in ASD we explored the link between symptoms of ASD on the one hand and ERN, Pe and post error slowing on the other hand. Given that previous studies found a relation between intellectual functioning and self monitoring (Rabbitt, 1990; Henderson et al., 2006), we also examined the relation between IQ and the ERN, Pe or post-error slowing.

Materials and Methods

Participants

A total of 18 controls and 25 ASD children took part in this study. From the control group 1 child was excluded because of bad electroencephalographic (EEG) data, 1 because of misunderstanding the task and 6 because of not passing the criteria of 5 error trials which was necessary to be included in the analysis. From the ASD group, 1 child was excluded because of unclear diagnosis and 7 children were excluded because of not passing the criteria of 6 error trials. The final group consisted of 10 control children (ratio male: female: 10:0; mean age: 9.23 years; SD: 1.20) and 17 children with ASD (ratio male: female: 16:1; mean age: 10.42 years; SD: 2.04). Clinical and comparison participants were matched on age at the group level ($F(1, 25) = .962$, $p = .336$). The children with ASD were recruited from the department of child and Adolescent Psychiatry at the Utrecht Academic Hospital. Controls were recruited from elementary schools in and around Utrecht and had no history of medical or psychiatric problems. Groups did not differ in IQ (Wechsler Intelligence Scale for Children (WISC-RN) (see Table 1). All diagnoses were based upon DSM-IV criteria and were made by a child psychiatrist after extensive diagnostic evaluation, including a review of prior records (developmental history, child psychiatric and neurological observations and tests and neurological investigations). The patients' diagnosis were either autism (n =10) or Asperger syndrome (n =7) based on DSM-IV criteria (American Psychi-

atric Association, 1994) and ADI-R (Lord, Rutter & Le Couteur, 1994). The ADI-R is a semi-structured interview for caregivers of children and adults with ASD and consists of three domains: a) quality of social interaction b) communication and language and c) repetitive and restricted and stereotyped interests (Lord et al., 1994). Two of the patients with Asperger syndrome did not meet the strict ADI criteria for autism on one of the domains. All subjects were medication free (medication was never prescribed) and had no significant neurological history. The experiment was approved by the local ethical committee and parents gave written informed consent. The study conformed with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Table 1. Mean FS (Full Scale), Performance (P) and Verbal (V) IQ scores for ASD children and Controls.

	FS IQ	PIQ	VIQ
ASD	94.5 (16.2) *61-120*	99.19 (17.9) *59-129*	92.19 (15.3) *64-112*
Controls	95.1 (12.5) *81-116*	100.6 (14.3) *73-118*	90.8 (10.8) *77-114*

Note. Standard deviations in parentheses, range in italics

Tasks

The current study is part of a larger project on executive functioning in children and adults with ASD by Hoeksma, Kemner, Verbaten and van Engeland (2004). The dual task design was chosen in light of this study to investigate processing capacity in children and adults with ASD. It is unrelated to the rationale behind the present study, which investigates self-monitoring related to ACC functioning. In this paper only the electrophysiological measures relevant for error processing are reported, the other components that are elicited by the auditory decision task have been reported elsewhere (Hoeksma et al., 2004)

In the task, the participants were administered an easy and a hard version of an auditory decision task, each consisting of two blocks. In the easy task, each block contained 70 task stimuli, which were animal sounds of a cat, dog, sheep and pig. These stimuli were presented binaurally through in-ear phones, at a level of 95 dB. In the easy task, the subject's instruction was to press a right-hand button whenever a cat sound was presented and a left-hand button for every other sound. In this condition there were 34 cat sounds and 36 non-cat sounds for each block to ensure approximately as many right- as left-hand button presses. In the hard task, the animal sounds were evenly divided. In this condition, the subject's task was to compare each sound that was presented with the preceding sound. When the sound was the same as the preceding sound, the subject was instructed to press the right-hand button. When the sounds were dissimilar, the left-hand button was to be pressed. To ensure as many right- as left-hand button presses, the probability that two successive stimuli were (dis-)

similar was 50%. Thus, for proper execution of this task condition, subjects had to keep a running memory of presented stimuli. In both the easy and hard condition all auditory task stimuli were task relevant, since they all required either a right- or left-hand button press. Visual probes were presented in the center of a computer screen, in between presentations of auditory task stimuli. There were 70 probe stimuli per block, divided into three stimulus types. Standards (60%) were abstract figures, composed of black and white squares. The information value of each figure was 80 bits (Attneave, 1954). Deviants (20%) were adapted from the standard stimuli, but the stimuli were divided into four evenly large quadrants, which were each mirrored and rotated 180°. Novels (20%) were unique abstract colored patterns. Each novel occurred only once in the entire experimental session. All visual stimuli were presented on a computer monitor, which was positioned at about one meter from the subject's eyes. Standard and deviant probes subtended a height of 5.7° of arc and a width of 11° of arc. Novels subtended a height of 10.5° of arc and a width of 11.75° of arc. All stimuli were presented with a duration of 0.3 seconds. Interstimulus intervals (ISIs) between primary (auditory) task stimuli were randomized between 4.2 en 5.4 seconds. Probe stimuli were presented following a task stimulus with an ISI varying randomly between 1.95 and 2.55 seconds. Subjects were told that in between task stimuli, pictures would appear on the screen; these required careful attention, but no response. Instructions for the tasks were given orally, and the subject had to perform a short practice series during which the experimenter followed the subject's responses on-line. When the experimenter was convinced that task requirements were met, the subject was instructed to move as little as possible during the task and to keep his eyes fixed on a crosshair on the center of the computer screen. After each task block, the experimenter entered the room and gave instructions for the next block.

Electrophysiological recording, data reduction, source analysis and statistical analysis

The EEG was recorded with a 62-channel electrode cap, including a left mastoid reference. EEG epochs were extracted beginning 1100 ms before and ending 900 ms after each *response* using the SCAN software package (Neuroscan, version 4.2). The epochs were band pass filtered with a 30Hz, 24 dB/octave low pass filter and baseline corrected using a pre-response window of -1100 – -900 ms. Vertical eye movements and blinks were removed from the data by application of a linear regression procedure (Semlitsch, Anderer, Schuster & Presslich, 1986). In a next step epochs containing artifacts exceeding 125 μV were excluded from further data analyses. To ensure enough error trials for analyses; the data from easy and hard tasks were combined. Finally, to quantify the ERN and the Pe, the epochs were averaged time-locked to the response, separately for trials to which

subjects responded correctly and incorrectly. The mean number of trials that went into the averages for correct and incorrect trials were 171 (SD: 64) and 13 (SD: 7) for controls and 178 (SD: 57) and 15 (SD: 8) for children with ASD. There was no significant difference between the groups with respect to the number of correct and incorrect trials. It was recently pointed out (Thomas, Grice, Najm-Briscoe & Miller, 2004) that when fewer than 27 trials are used for averaging of ERPs, the signal-to-noise ratio is low and this results in systematic overestimation of peak amplitudes. This might be the case with respect to erroneous responses, as few trials went into the averages compared to correct responses. In the present study however, we used mean areas because they do not become biased by differences in Signal to Noise Ratio (SNR) and are therefore allowed to use when comparing conditions containing unequal numbers of trials (Luck, 2005). In addition to using mean areas, we checked whether we could replicate our results when comparing incorrect trials with a set of randomly selected correct trials, which were matched in number to the number of incorrect trials. This was the case for all of our analysis (see appendix A). Finally, given the small number of erroneous trials needed to be included in the analysis ($n > 5$) and the known influence of number of trials on average ERP amplitude, we explored whether there was relationship between the number of trials and the size of the ERN and Pe. We did not find evidence for this and therefore did not include number of trials as a covariate in our analysis.

We measured the amplitude of the ERN by computing the difference between the mean area amplitude in a window surrounding the first positive peak preceding the response (mean area: 110-50 ms before the response) and the mean area amplitude surrounding the first negativity after the response (mean area 30-70 ms) at Fz and FCz for correct and incorrect averages separately. We analyzed the ERN using a 2 (Group: ASD/control) x 2 (Trial Type: correct/error) x 2 (Electrode: Fz/FCz) mixed ANOVA. The amplitudes of the Pe (mean area measure: 250-500 ms after response at Cz and Pz; see Figure 1) were measured per lead, using a 2 (Group: ASD/control) x 2 (Trial Type: correct/error) x 2 (Electrode: Pz/Cz) mixed ANOVA.

Post error slowing in reaction times was analyzed by comparing the mean reaction time (RT) of correct trials following either correct or error trials (2 (Group: ASD/control) x 2 (Slowing: correct-correct; error-correct) mixed ANOVA). Furthermore, planned contrasts were performed to test the hypotheses that controls would show significant post-error slowing, whereas children with ASD would not.

For the ERN, Pe as well as post-error slowing we investigated whether there was a significant correlation with total IQ scores, verbal IQ scores and performal IQ scores as well as symptom presentation on the three domains of the ADI-R using Pearson-R.

To explore whether the sources of the ERN could be localized to the same brain region (ACC) in children with ASD and controls, for each group (ASD/Controls) the locations of the neural generators for the ERN were modelled on the grand-average average-referenced ERN data for incorrect responses, using Brain Electrical Source Analysis software (BESA2000; www.besa.de). For source modelling a four shell ellipsoidal head model was used. Because bone thickness and conductivities are age dependent, the default (adult) values were adjusted to 5.7 mm for bone thickness and 0.012 for bone conductivity. All reported dipole solutions were obtained without constraints and were stable across randomly varying starting positions.

Results

Reaction times: Post-error slowing

Controls and children with ASD did not differ in the number of errors (controls: 14.4 (SD: 7.23; range: 6-29); ASD: 21.41 (SD: 13.34; range: 5-60)) or in mean reaction time (controls: 919 ms (SD: 196 ms); ASD: 973 ms (SD: 98 ms)). Planned contrasts indicated significant post error slowing in controls only ($t(9) = 2.472$, $p < 0.05$). In controls, the mean RT for correct trials was significantly longer following error trials than following correct trials (Mean difference: 69 msec; SD: 88 ms). In children with ASD slowing was not significant (Mean difference: 20 msec; SD: 103 ms). There was no relationship between post-error slowing and IQ measures or symptom presentation.

ERN

Analysis of the three-way ANOVA indicated a significant interaction between Trial Type and Group ($F(1, 25) = 7.99$, $p < 0.01$), suggesting that the difference between correct and incorrect trials differed between the groups. Further analysis of this interaction showed that there was a significant difference between correct and incorrect trials in controls only ($F(1, 9) = 8.35$, $p < 0.05$). Children with autism showed a smaller Error Related Negativity compared to controls ($t(25) = -3.11$, $p < .01$), whereas there was no group difference in negativity with respect to correct responses (see figure 1 and table 2). Finally, there was a main effect of electrode ($F(1, 25) = 16.72$, $p < 0.001$) with larger amplitudes for FCz than Fz in children with autism as well as controls. There was no relationship between ERN amplitude and IQ measures or symptom presentation.

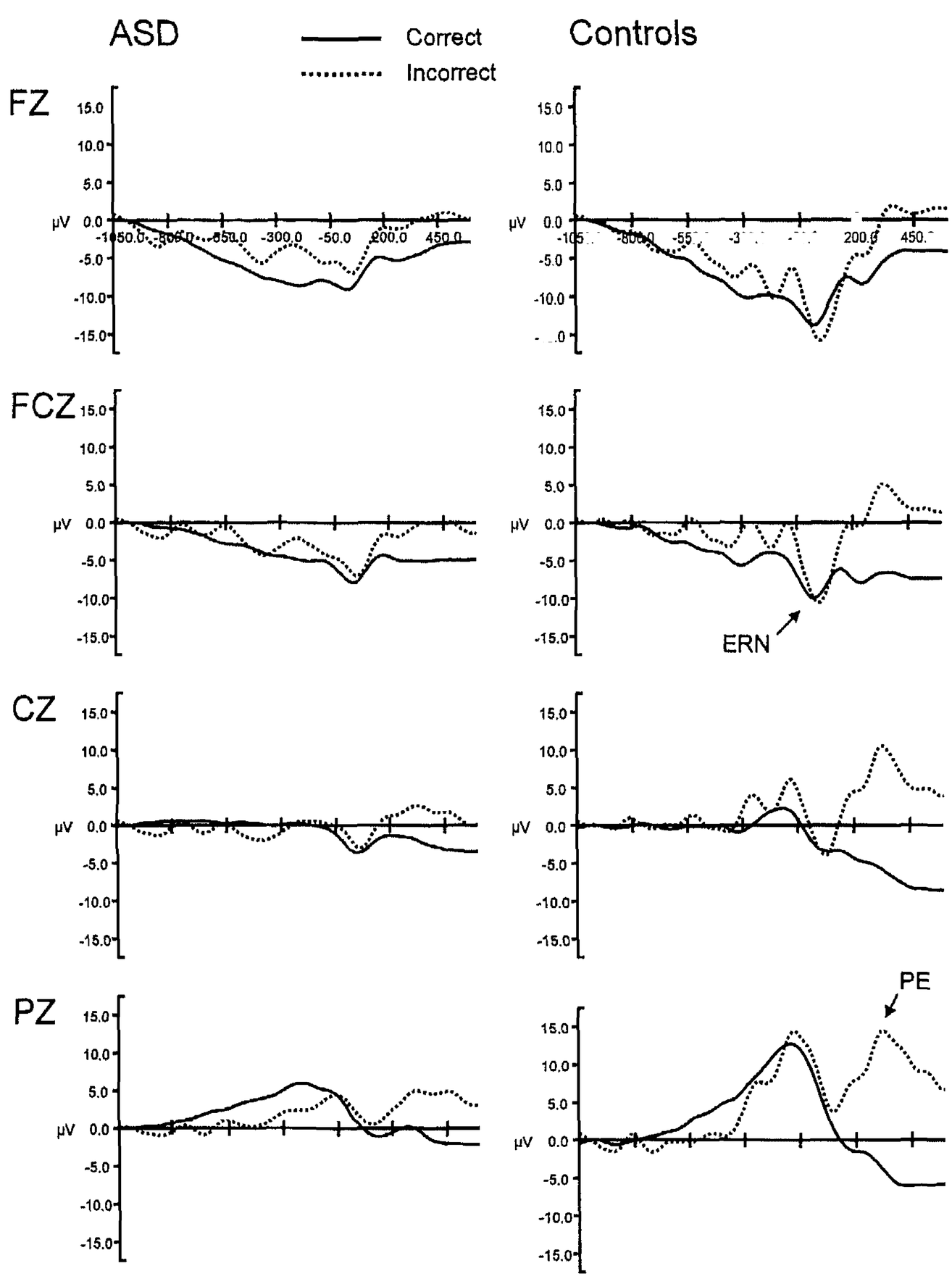

Figure 1. Grand averaged response-locked waveforms for normal controls and children with ASD.

Table 2. Mean amplitude (area) (SD in parentheses) for the ERN and the Pe on correct and incorrect trials for children with ASD and controls

	Correct		Incorrect	
	Fz	FCz	Fz	FCz
ERN amplitude (μV)				
Controls	-2.24 (4.81)	-5.16 (4.12)	-11.67 (9.99)	-12.89 (10.99)
ASD	-1.49 (4.46)	-3.12 (4.26)	-1.57 (6.52)	-3.01 (6.66)
	Correct		Incorrect	
	Cz	Pz	Cz	Pz
Pe Amplitude (μV)				
Controls	-6.49 (5.26)	-4.53 (4.66)	8.12 (14.23)	12.55 (14.33)
ASD	-2.29 (4.73)	-1.48 (5.69)	2.14 (8.85)	4.66 (9.22)

Importantly, as the ERN was measured peak-to-peak (with a mean area measure around the peaks), we checked whether the difference in ERN activity between children with ASD and controls could be explained by a group difference in the initial positivity, that took place prior to responding. Results showed that children with autism and controls did not differ in the initial positivity at Fz or FCz on correct as well as incorrect trials.

Pe

Analysis of the three-way ANOVA indicated a significant interaction between Group and Trial Type irrespective of electrode ($F(1, 25) = 7.97$, $p < .01$). Both controls and children with ASD showed a larger positivity after an error than a correct response (Controls: $F(1, 9) = 21.09$, $p = 0.01$; ASD: $F(1, 16) = 6.07$, $p < 0.05$). This effect was however reduced in children with ASD (see figure 1 and table 2). In addition, there was a main effect of electrode ($F(1, 25) = 8.62$, $p < .01$) with larger amplitudes at Pz. There was no relationship between the Pe and IQ measures or symptom presentation.

Source Analyses

In controls, a one-dipole source model was obtained after source analysis of the ERN for incorrect trials (see figure 2). The dipole was located in the dorsal region of the ACC and accounted for a large part of the variance in the observed data (ERN location (Cartesian coordinates): x -.04, y -.02, z .43); residual variance (RV): 4.6%; dipole strength: -67.57 nAm). In children with ASD a one dipole source model was also obtained. The source was located in a similar location in the ACC (x -.07, y -.05, z .51), compared with controls, but the variance that this

model explained was reduced (RV: 19.6 %) as well as it's strength (-25.87 nAm). Extending the model with an extra dipole in children with ASD did not result in a reliable source model. Because a negativity was observed on correct trials as well, the source of this activity was also modelled. In controls the dipole was located in the dorsal region of the ACC (location: x -.08, y -.20, z .43; RV: 7.9%; dipole strength: -55.01 nAm). In children with ASD the source was located in a similar location (x -.01, y .29, z .51), but again the variance that this model explained was reduced (RV: 22.7%) as well as its strength (-23.38 nAm). Extending the model with an extra dipole in children with ASD did not result in a reliable source model. Since the grand-average average-referenced Pe did not have a clear maximum, neither in ERP amplitude, nor global field power, the sources could not reliably be detected.

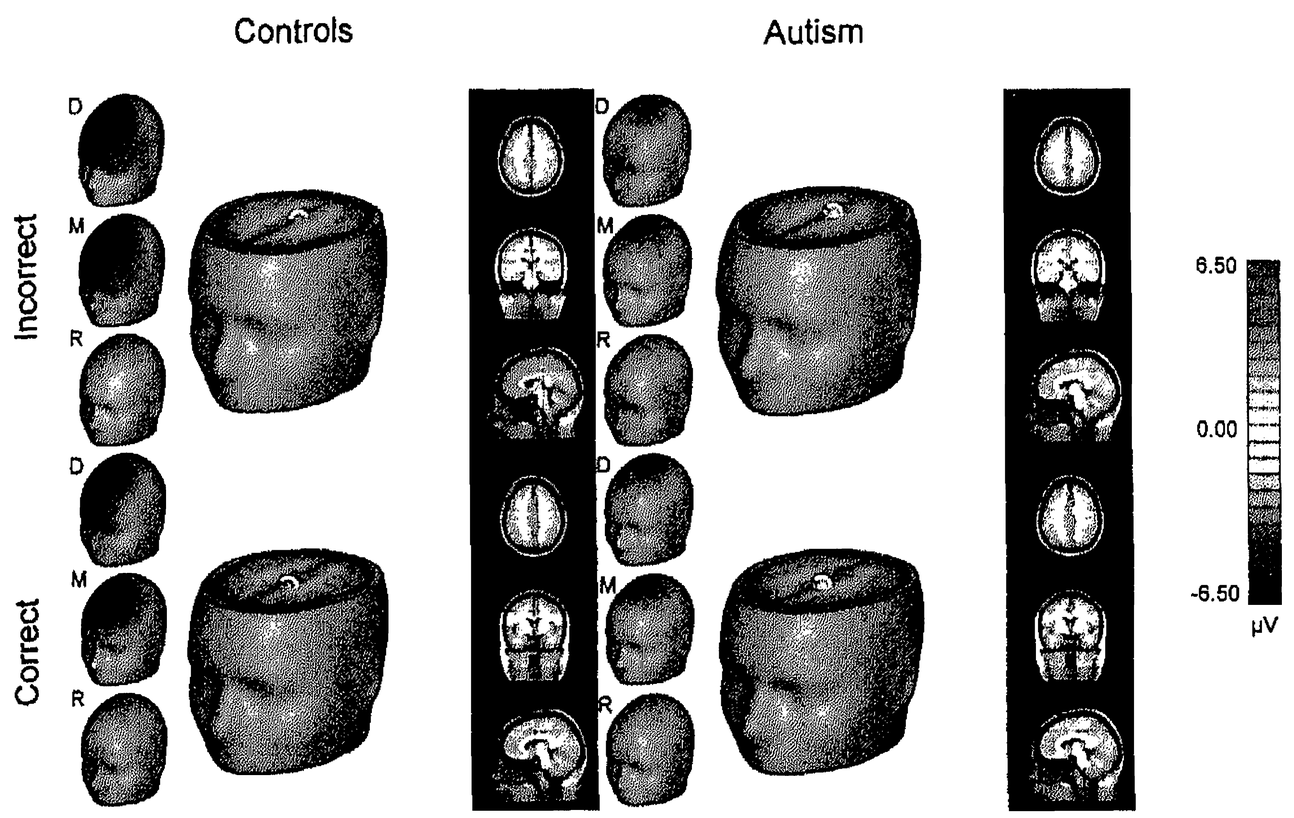

Figure 2. Dipole source models, derived at ERN peak latency of the average-referenced group-averages for controls (red) and children with ASD (blue) for correct and incorrect responses, projected on a standard realistic MRI head model. The dots in the MRI head models represent source location, whereas the line represents source orientation. The voltage scalp distribution maps (left) indicate: (D) the voltage distribution of the original data, (M) the voltage distribution explained by the model and (R) the residual scalp distribution. Transversal, coronal and sagittal views of the dipole, projected on a standard realistic MRI head model, are shown on the right. All dipoles are located in the ACC region.

Discussion

Our study aimed to investigate ACC functioning in children with ASD, compared to age- and IQ matched controls, by measuring behavior and ERP activity related to self monitoring. We found that only control children showed significant post-error slowing, indicating that children with ASD show less adjustment in response strategy after an error. A lack of post-error slowing has been recently reported in adults with ASD as well by Bogte, Flamma, van der Meere and van Engeland (2007). Error signals provide crucial information for adjustment in a continuously changing environment. The finding that children with ASD do not adjust response strategies according to response outcome might contribute to the enhanced perseverative and rigid behavior that is characteristic for children with an ASD diagnosis (Lord, Rutter & Le Couteur, 1994). Errors of perseveration have been reported before in go-no-go tasks in ASD (Ozonoff, Strayer, McMahon & Filloux, 1994).

In addition to post-error slowing, control children showed a significant ERN, which could be localized in the ACC, as has been reported before in other studies (Luu et al., 2000; Hermann et al., 2004; van Veen & Carter, 2002; O'Connell et al., 2007). A negativity localized to ACC was also seen after correct trials (CRN), although it was significantly larger after error trials. Usually, a negativity is present only after incorrect trials, but is has been reported for correct trials as well in dual tasks, like the present task (Pailing & Segalowitz, 2004). The suggestion is that dual tasks evoke task uncertainty, thereby causing response conflict on both correct and incorrect trials (Pailing & Segalowitz, 2004). Furthermore, the CRN has been found to be larger in children than adults, which might reflect additional uncertainty about the response (Davies, Segalowitz, & Gavin, 2004).
Importantly, children with ASD did not show a significant difference in negativity between correct and incorrect trials. This was due to ERN activity, localized in the ACC in both groups, being smaller in children with ASD on incorrect trials. As the ERN was measured as the difference between the positivity preceding and the first negativity following the response, it was verified that these group differences were indeed caused by differences in the negativity and not the positivity. The functional significance of this pre-ERN positive component is unclear. It might reflect stimulus related P3 activity (Davies, Segalowitz, Dywan & Pailing, 2001) but has also been linked to phasic synchronization of theta activity before response onset (Luu et al., 2004). The difference between ASD children and controls in ERN amplitude can neither be explained by differences in number of error trials since this was comparable between the groups.

In contrast to the present study, a recent study reported larger ERN amplitudes, compared to control children in children with ASD that had a verbal IQ > 103 (Henderson et al., 2006). In the present study however, there was no relationship between Verbal IQ, diagnostic group and ERN amplitude. The results of

the present study and the study of Henderson et al. (2006) are difficult to compare, because in the latter study a substantial part of the ASD group was on medication as opposed to in the present study. In addition, different tasks were used in both studies. Finally, in the study of Henderson et al. (2006) the Pe was not investigated and no information was provided on the underlying dipole sources.

One possible explanation for the smaller ERN in ASD children in the present study might lie in different experiences of task complexity. In a developmental study, adolescents showed a reduced ERN compared to adults in a complex task, but not in an easy task (Hogan, Vargha-Khadem, Kirkham & Baldeweg, 2005). The authors suggested that increased task demands in the complex task might cause recruitment of other brain regions that influence the ERN generator differently than in easy tasks. However, such an explanation seems unlikely since children with ASD and controls did not differ in reaction times and number of errors on the task. Because of the presence of an ERN-like component also on correct trials (CRN), there is growing consensus that, instead of being specific to error detection per se, the ERN is a reflection of continuously active performance monitoring processes that are enhanced on error trials (Vidal, Hasbrouc, Grapperon & Bonnet, 2000). In line with this, Brown and Braver (2005) suggest that the primary role of the ACC, the generator of the ERN (Luu et al., 2000; Hermann, Römmler, Ehlis, Hedrich & Fallgater, 2004; van Veen & Carter, 2002), is the detection of situations in which there is an increased likelihood of making errors rather than error detection in itself. The finding of ACC sources underlying both CRN and ERN in the present study supports such a conclusion. Following the above functional interpretations of CRN, ERN and ACC, the reduced ERN in children with ASD might suggest a specific insensitivity to detect situations in which the chance of making errors is enhanced. This might in turn lead to a failure in the recruitment of coping strategies to deal with this situation, i.e. a failure to allocate more attention, as becomes evident from the lack of post-error slowing in the ASD group.

Besides the reduced ERN, children with ASD also had a reduced Pe response (enhanced positivity to error trials compared to correct trials) compared to age-matched controls. In previous studies including healthy adults, the Pe has been linked to the consciousness or awareness of error processing (Nieuwenhuis, Ridderinkhof, Blom, Band & Kok, 2001; O'Connell et al., 2007). The reduced Pe in children with ASD, therefore, suggests impairments in the conscious processing of the error event. Such reduced error awareness might prevent children with ASD from adapting future behaviour, as reflected in the absence of post-error slowing in children with ASD. Overbeek, Nieuwenhuis and Ridderinkhof (2005) however found limited evidence for a link between the Pe and post error slowing. Another explanation for the reduced Pe in ASD children might be a reduction in the perceived emotional significance of an error (Overbeek et al., 2005) or it

might reflect a general reduction in allocation of attention to important events that is not specific to errors (Jonkman, van Melis, Kemner, & Markus, 2007). The latter explanation would be in line with an interpretation of the reduced ERN (in the presence of intact CRN) reflecting an insensitivity to detect situations with increased likelihood of making errors, preventing the recruitment of effective coping strategies.

It is important to view the present results in light of the developmental literature in this field. Several developmental studies have found that typically developing children (Wiersema et al., (2007): 7-8 years; Davies et al., (2004): 7-12 years), show a reduced ERN compared to adults. In addition, several fMRI studies have shown an increase in ACC activation from childhood to adulthood (Adleman et al., 2002). Ladouceur, Dahl & Carter (2007) state that this increase in level of activation may be related to stronger or more synchronous firing of neurons in the ACC, which could explain the increase in ERN amplitude. Alternatively, Ladouceur et al. (2007) suggest that with age the ACC might become more sensitive to errors or response conflict. Others have implicated the late development of the mesensephalic dopamine system which has been suggested to convey negative reinforcement signals to the frontal cortex, where the ERN is generated in the ACC (Davies et al., 2004; Wiersema et al., 2007).

In light of these developmental findings, the reduced ERN in children with ASD may reflect immaturity or impaired functioning of the ACC and/or connected regions and/or related neurotransmitter systems. This might cause an insensitivity to detect situations which increased likelihood of making errors in children with ASD, eventually preventing the recruitment of effective coping strategies. Deficiencies in ACC functioning have been found before in adults with ASD. One study reported decreased metabolism in the ACC (Haznedar et al., 1997; Haznedar et al., 2000) and, two other studies have shown a relation between ACC metabolism and social impairments in ASD (Haznedar et al., 2000; Ohnishi et al., 2000).Future studies should investigate whether deficits in the early stages of error monitoring are present in adults with ASD as well. This might set light on whether the reduced ERN in children with ASD is a reflection of a developmental delay or might be present during the entire lifespan.

Besides a link to the ACC, the present findings on impaired self-monitoring as reflected by the ERN and Pe might be linked to the problems of subjects with ASD to meet the requirements of social interactions. Several behavioural features in ASD, like perseverative responding, repetitive behaviors, poor imitation skills, and joint attention impairments, may all involve an inability to consistently and accurately monitor ongoing behaviors (Hill, 2004; Mundy, 2003; Russell, 1997; Henderson et al., 2006). Furthermore, it has been suggested that if children develop difficulties in self-monitoring early in life, they fail to enjoy the normal experiences of being responsible for their actions, resulting in an impoverished sense of self and eventually a failure to develop a normal theory of mind (Rusell

& Jarrold, 1998). Unfortunately we did not find a relationship between the ERN, Pe or post error slowing and symptom presentation. This might be due to the relatively small sample size and needs further investigation.

Regarding the specificity of the current findings, previous research has indicated reduced post-error slowing and Pe in ADHD children, concurrent with a normal ERN (Wiersma et al., 2005; Jonkman et al., 2007), although a reduced ERN in children with ADHD has been reported in another study (Liotti, Pliszka, Perez, Kothmann & Woldorff, 2005). In schizophrenia patients normal post-error slowing and Pe have been found, but the ERN has been found to be smaller in size (Mathalon, Fedor, Faustman, Gray, Askari & Ford, 2002). A similar pattern has been reported for low-socialized adults and children (Santesso, Segalowitz & Schmidt, 2005). In patients with obsessive-compulsive disorder a normal Pe and an increased ERN is found (Gehring, Himle & Nisenson, 2000). Based on these studies, a reduced ERN, Pe and post-error slowing seems to be quite specific to ASD, although there might be overlap with ADHD. Additional research in ASD and ADHD needs to further investigate this suggestion.

Importantly, the sources of the ERN could be located in the ACC area in the present study, in accordance with other studies (Luu et al., 2000; Hermann et al., 2004; van Veen & Carter, 2002). Therefore, this study provides direct evidence for abnormal ACC activation, related to self monitoring (i.e. error-monitoring) behavior in ASD. The higher percentage of residual variance that remained after source modeling in children with ASD compared to controls, might hint to additional activity in brain areas other than the ACC during error processing in children with ASD. It could be that children with ASD show large individual differences in the additional areas they activate during error processing. This might be a reason why it was not possible to fit a second dipole at the group level, and might explain the large residual variance in the ASD group.

In sum, we found evidence for reduced self-monitoring in ASD as reflected by a reduction in ERN, Pe and post-error slowing. Reduced monitoring (ERN) in the early stages of error processing might be linked to impaired/immature functioning of the ACC and connected regions in ASD, and might reflect an insensitivity to detect situations in which the chance of making errors is enhanced. The reduced Pe in children with ASD probably reflects reduced error awareness or a reduction in allocation of attention to erroneous events. Behaviorally, these deficiencies are reflected in a lack of post-error slowing in children with ASD.

Appendix A

Results of the 3-way ANOVA with factor Trial Type (correct/incorrect), Electrode (ERN: Fz, FCz and Pe: Cz, Pz) and Group (controls/ASD). Instead of including all correct trials, mean amplitudes for the correct trial type were based on a random set of correct trials, matched in number to the number of incorrect trials for each subject.

Source	Df	F/t	P
ERN			
3-way ANOVA (Fz, FCz)			
Trial Type x Group	1, 25	F = 5.54	.03
Electrode	1, 25	F = 27.05	< .001
Trial Type per group			
ASD: Correct-Error	1, 16	F = .15	.71
Controls: Correct-Error	1, 9	F = 6.58	.03
Group per Trial Type			
Error: Controls-ASD	25	t = -3.12	< .01
Correct: Controls-ASD	25	t = -.78	.44
Pe			
3-way ANOVA (Cz, Pz)			
Trial Type x Group	1, 25	F = 8.81	< .01
Electrode	1, 25	F = 4.92	.04
Trial Type per Group			
ASD: Correct-Error	1, 16	F = 5.82	.03
Controls: Correct-Error	1, 9	F = 12.46	< .01

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General discussion, conclusions and implications for future research.

6

Chapter 6

General aims

Rapidly perceiving the emotional content of a face is an important skill for successful social behavior, since it helps to evaluate the states and intentions of others and to adapt future behavior accordingly. One of the ways in which the visual system captures environmental information, like facial expressions, is in terms of luminance variations that vary across space. High spatial frequencies (HSF) represent abrupt, small luminance changes, corresponding to sharp edges and fine perceptual detail. Low spatial frequencies (LSF), on the other hand, represent global changes in luminance, and provide information about the general shape, proportions and large contours of objects in our visual environment (Bar, 2004; Goffaux & Rossion, 2006; Morrison & Schyns, 2001). Several studies in adults have indicated that particularly LSF information plays an important role in the rapid processing of facial expressions (e.g. Pourtois, Dan, Grandjean, Sander & Veuilleumier, 2005; Holmes, Green & Vuilleumier, 2005). Some studies have proposed a rapid subcortical face processing pathway which is preferentially tuned to LSF and modulates activity in visual areas to provide early signals of, for example, threat (Pourtois et al., 2005; Veuilleumier, Armony, Driver & Dolan, 2003).

This perceptual side of facial expression processing is often overlooked, and is hardly taken in consideration when studying the development of normal and abnormal processing of facial expressions. This is however of crucial importance, considering that facial expressions form the basis for communication and social development early in life when language is relatively immature. Any abnormalities in low level visual perception early in life could lead to difficulties with processing emotional expressions from faces and, as a consequence, might lead to abnormalities in social interaction. Such basic visual processing deficits have recently been suggested to underlie the face processing difficulties that have been found in children with Autism Spectrum Disorder (ASD) (Johnson, 2005; Behrmann, Thomas & Humphreys, 2006).

The **first aim** of this thesis was to explore whether typically developing children show developmental changes in the type of spatial frequency information, (i.e. HSF and/or LSF) that is used to process facial expressions between ages 3-8. (chapter 2).
The **second aim** was to examine whether 3-4 year-old children with ASD show abnormalities in visual processing of HSF and LSF information and investigate the role that both play in facial expression processing (chapter 3).
The **third aim** was to address the role of SF in facial expression processing in adulthood, because previous studies including adults showed controversial results. In addition, a methodological question related to the way in which the

present and previous studies have manipulated the SF content of facial expression images, was investigated (chapter 4).
The **fourth aim** was to investigate a specific aspect of executive functioning, the ability to self-monitor actions, in older children (mean age: 10 years) with ASD (chapter 5).

To address these questions Event Related brain Potentials (ERPs) were used because they are well-suited to 1) study the different stages of facial expressions and SF in the visual cortex because of its high temporal resolution. 2) apply in young children and especially clinical groups, because they do not require behavioral or verbal responses. In this chapter the main findings of the experiments described in this thesis will be discussed.

6.1 Developmental patterns in the type of spatial frequency information that is used for facial expression processing

Previous studies in healthy adults have shown that early visual cortical responses to emotional face expressions are primarily mediated by LSF information (Pourtois et al., 2005; Winston, Vuilleumier & Dolan, 2003; Vuilleumier et al., 2003). Chapter 2 explored whether there are developmental differences in the type of spatial frequency information (HSF and/or LSF) that is important for facial expression processing in typically developing children (3-8 years). To investigate this, we recorded visual brain responses from three different groups of children differing in age (3-4, 5-6 and 7-8 year-olds) while they passively viewed pictures of neutral and fearful faces, containing either HSF or LSF information. More specifically, two ERP components that index relatively early stages of facial expression processing in visual areas were analyzed: the P1 and N170. The P1 (positivity at 100 ms after Stimulus Onset (SO)) is a fast exogenous response, which reflects striate as well as extrastriate visual processing (e.g. Rossion et al., 1999). The N170 (negativity at 170 ms after SO) originates from a network of regions, probably including the fusiform gyearus, inferior occipital cortex, superior temporal sulcus and the inferior, middle and superior temporal gyeari (Henson, Goshen-Gottstein, Ganel, Otten, Quayle & Rugg, 2003). The N170 is thought to be a marker of face detection, but also face encoding processes, such as the encoding of the structure or configuration of the face (e.g. position of the eyes relative to the mouth), that are important for the ability to discriminate between different faces (Jacques & Rossion, 2006).

In contrast to previous findings in adults (Pourtois et al., 2005), the developmental ERP study described in chapter 2, indicates that in 3-8 year-old children the processing of fearful facial expressions in visual areas is primarily

driven by HSF information. In chapter 2 no evidence for developmental differences between 3-4, 5-6 and 7-8 year-old typically developing children was found. In chapter 3 however, we found that 3-4 year-old children with a developmental delay, which served as a control group for the 3-4 year-old ASD children, *did* show an LSF bias during the first stage (at the P1) of emotional expression processing in the visual cortex. In this respect, results from chapter 2 and 3 seem to be in conflict with each other with respect to the youngest age group, the 3-4 year-olds.

Such inconsistencies between the studies with respect to this initial processing stage might be related to differences in chronological and mental age between the groups. That is, the 3-4 year-olds in the study in chapter 3 had a developmental delay of one year, whereas the mental age of the typically developing 3-4 year olds that took part in the study described in chapter 2, matched their chronological age. However, a closer look at figure 3b in chapter 2 shows that the early visual processing (P1 effect) of fearful expressions, is also primarily driven by LSF information in healthy 3-4 year-olds without a developmental delay. Although this did not reach significance in the overall statistical analysis , including all age groups (3-8 years; see chapter 2), a separate test of the spatial frequency x emotion interaction on the P1 in the 3- and 4-year-olds only, showed that the processing of emotion was indeed primarily driven by LSF in this age group. This effect was of similar size as in the children with a developmental delay. At a later stage of processing in visual cortex, as indexed by the next ERP component (the N170), emotion processing in 3-4 year-olds was primarily driven by HSF information as in the older children.

In sum, the following developmental pattern is observed: in 3-4 year-old children, the first visual cortical response (P1) to fearful expressions that was measured was mediated by LSF information, whereas at a later processing stage (N170) emotion processing was driven by HSF information. In contrast, in older children (5-8 year-olds), the processing of fearful expressions in the visual brain was mediated by HSF information at both early and late processing stages (P1 and N170). Finally, in adults, fearful expression processing in visual cortex was shown to be primarily mediated by LSF information, as shown by Emotion x SF effects at both P1 and N170 level (see Pourtois et al., 2005 and chapter 5). In the next paragraph, some possible explanations for this developmental pattern will be given.

In adults, rapid processing of emotional information in visual cortical areas has been suggested to be initiated by connections with a subcortical face processing pathway, or 'shortcut', which includes the amygdala and is preferentially tuned to LSF (Pourtois et al., 2005; Veuilleumier et al., 2003). Based on the finding that in (older) children emotional effects were primarily driven by HSF information, we have suggested in chapter 2 that the subcortical LSF pathway, or the communication between this pathway and the cortical areas, might not be

fully mature in childhood. Indeed, there are indications from animal models that amygdala-cortical connectivity continues to mature into adolescence, at least in the prefrontal areas (Cunningham, Bhattacharyya, & Benes, 2002). This explanation is, however, difficult to reconcile with findings in the 3-4 year-olds, in which early processing of emotion was primarily driven by LSF.

An explanation that takes into account both the maturation of the visual system and the influence of developmental differences in expertise with face processing might better fit the data from both chapter 2 and 3. The literature on visual system maturation shows that the ability of the visual system to resolve HSF information has not fully reached maturity at the age of 3-4 years (e.g. Mayer & Dobson, 1982). Possibly, due to this immaturity, relevant emotional cues cannot be rapidly resolved from HSF information, and this might explain why in the youngest 3-4 year-old children, the first stage of cortical facial expression processing (P1) is based primarily on LSF information. At the age of six years however, the ability to resolve HSF information is fully mature and HSF information (e.g. forehead wrinkels, eye size, mouth region) might be most efficient for the rapid extraction of emotion in school age children (at least up to 8 years) in both the early and later stages of processing (chapter 2). A previous study (Pourtois et al., 2005) and the study described in chapter 5 showed that in adults, emotion expression processing was mediated by LSF information at both early (P1) and later (N170) face processing levels in visual cortex. This developmental shift to the use of LSF cues at both P1 and N170 levels, might be related to increased expertise with face processing in adulthood. There is some evidence supporting such an hypothesis. For example, an experiment of Schyns & Oliva (1999) showed that when adults were familiarized with faces by training, they more frequently used LSF information for face identification. Such an interaction between experience and spatial frequency has also been noted in a behavioural study on tool expertise (Viggiano, Righi & Galli, 2006). Viggiano et al. (2006) showed that in tool-experts, who have experienced prolonged exposure to tools, a small amount of LSF information in tool pictures was sufficient for tool identification in contrast to novices who performed best for stimuli containing HSF information. These results thus suggest that when visual (face) processing becomes more automatic because of enhanced experience, there is a shift towards the use of LSF information for the extraction of relevant stimulus (face) features. Based on this literature, we suggest that the initial use of HSF information for fast cortical processing of fearful expressions during childhood (5-8 years) is due to a combination of maturational constraints of the visual system and relatively low expertise with face processing. During later childhood, with increasing expertise in the processing of different facial expressions, we suggest a shift will occur to the use of LSF cues at both early (P1) and later (N170) face processing stages, as was the case in adults in the present study. This hypothesis could however not be tested in the present thesis because the maximum age of children

included was 8-years. With the use of LSF, facial expression processing becomes also more efficient because the visual system processes LSF faster compared to HSF (see for review Goffaux & Rossion, 2006).

It must be emphasized that it is, as yet, unclear whether the early LSF-based processing of fearful expressions in the youngest age group and in adults is mediated by a rapid subcortical processing route which includes the amygdala and modulates activity in the visual cortical areas (see Pourtois et al., 2005; Veuilleumier et al., 2003). It is well possible that this early, LSF-based, facial emotion processing in the visual cortex results from a rapid feedforward cortical projection within the visual system. Future studies, possibly using fMRI (or a combination of fMRI and EEG), should be aimed at further disentangling this. Furthermore it must be emphasized that we suggest that the LSF dominance in the first stage of emotional expression processing in the 3-4 year-olds, is of a different nature as the LSF dominance in both early and later processing stages in adults. As described in the previous paragraph, the latter possibly arises through an increase in face expertise whereas the use of LSF in the initial stage of processing in the 3-4 year-olds may be a reflection of immature HSF processing.

The above described developmental increase in the use of LSF information for cortical face processing, might be related to findings of behavioral studies that the relatively late development of the ability to use more global face information for determining a subjects age or identity.(Schwarzer, 2000). Schwarzer (2000) has for example shown that in younger children, face recognition depends on independent processing of different face features (local processing style), whereas with increasing expertise there is a shift towards the processing of faces as a whole, rather than as a collection of independent features (global processing style) (Young, Hellawell & Hay, 1987). Since LSF information has been shown to play a crucial role in global face processing (see for review Goffaux & Rossion, 2006), the mechanism behind the increased use of LSF information for emotion processing in the visual cortex in subjects with higher levels of expertise might be related to a change in perceptual processing styles from local (processing of separate features) to global (more integrated processing).

Increased use of global perceptual processing styles with development has also been reported for other types of visual information than faces. As reviewed by Scherf et al. (2008), several studies have reported that sensitivity to global structures in compound stimuli (e.g. a large shape (letter H) built up out of smaller shapes (letters x), is not fully mature even in late childhood. In global-local tasks in which such compound stimuli are presented, participants have to identify targets at a local (level of the smaller shape) or global level (level of the larger shape). Compared to adults, children show less interference from information at the global level when targets have to be detected at the local level. According to Scherf et al. (2008) these findings suggest that the ability to integrate local visual features spatially across the visual field shows a protracted development.

Importantly, just as is the case with global face processing, global processing of compound stimuli has been shown to be driven by the use of LSF information (Boeschoten, Kemner, Kenemans & Engeland, 2005; Shulman, Sullivan, Gish & Sakoda, 1986). Thus, it is well possible that the increased use of LSF information for visual processing with age might be a more general phenomenon and might be associated with developmental changes in local-global perceptual processing styles.

Whereas the ERP components that were investigated address the early stages of facial expression processing in the visual cortex, we also investigated whether there are developmental differences in the relative use of HSF and LSF information for facial expression processing at response level, by measuring reaction times in a rapid expression categorization task in the 5-6 and 7-8 year-old children. In this behavioral study, we did not find developmental differences in the use of LSF or HSF information when categorizing emotional expressions. In fact, results showed that children were faster in categorizing fearful, compared to neutral expressions, but this effect was present in both LSF and HSF conditions. It has to be noted that the ERP findings from the same group of children, showing emotion processing in the HSF condition only, did not correspond with these behavioral findings. The behavioral findings might indicate that in the latest stages of information processing (at response level), emotional (fearful) expressions are extracted on the basis of both LSF and HSF information in children. A recent behavioural study also reported that both HSF and LSF cues are used for emotion identification in typically developing children (one age group: 6-16 years) (Deruelle, Rondan, Salle-Collemiche, Bastard-Rosset & Da Fonséca, 2008).

6.2 Developmental effects in the processing of neutral facial expressions

In addition to the developmental effects in the role of SF in the processing of emotion, we also observed developmental differences in facial expression processing in general. In the behavioural categorization task, reported in chapter 2, the oldest (7-8 year-old) children correctly categorized a higher percentage of neutral faces than the younger children (5-6 year-olds). In agreement with this finding, Durand, Gallay, Seigneuric, Robichon, and Baudouin (2007) showed that the ability to recognize neutrality in faces continues to develop until 9 years of age. Below 9 years, children had the tendency to attribute an emotion (happiness or sadness) to neutral faces (see also Carlson, Felleman & Masters, 1983; Felleman, Barden, Carlson, Rosenberg & Masters, 1983; Reichenbach & Masters, 1983). Also, the results of the ERP studies in chapter 2 and 3 suggest that in typically developing children (3-8 years), 'neutral' faces might not be observed as

emotionally neutral as indicated by enhanced visual cortical activity in reaction to neutral, compared to fearful, faces. In support of the above mentioned studies, Thomas et al. (2001) demonstrated greater amygdala activity to neutral faces than fearful faces in children, whereas adults showed the opposite effect (see also Tottenham, Hare & Casey, in press). Thomas and colleagues (2001) argue that this difference between adults and children may be present because children observe neutral faces as being more ambiguous than fearful faces. Thus, on the basis of these results, it is hypothesized that neutral facial expressions are not yet perceived as neutral by children, and the enhanced cortical activity in response to neutral faces might be caused by enhanced effort invested in decoding the expression.

6.3 Abnormalities in SF and facial expression processing in ASD

As was discussed more elaborately in the introduction of this thesis, several studies have indicated a more detailed (visual) processing style in ASD, which might contribute to abnormalities in face processing (see for review Dakin & Frith, 2005; Behrmann et al., 2006). A number of behavioral studies found that HSF information is most important for face processing in adults as well as children with ASD, whereas controls also/primarily use LSF information, for example for identity matching (Deruelle, Rondan, Gepner & Tardif, 2004; Curby, Schyns, Gosselin, & Gauthier, 2003; Deruelle, Rondan, Salle-Collemiche, Bastard-Rosset, & Da Fonséca, 2008). In the present study, we investigated whether abnormalities in basic SF processing are already present early in life (3-4 years) in ASD and whether they affect face processing at this age. The processing of SF was investigated by presenting HSF and LSF grating stimuli. Concurrently, specific ERP peaks, that reflect early visual processing in the visual cortex, were measured. In addition, just as in the previous developmental studies, the role of spatial frequency in emotion expression processing in ASD was studied by presenting children with LSF or HSF-filtered faces with either a neutral or emotional expression. We presented these stimuli to 3-4 year-olds with and without ASD, and measured P1 and N170 activity.

Differences in basic visual processing of LSF and HSF using grating stimuli

Results showed that compared to controls, children with ASD show enhanced processing of HSF grating patterns in visual brain areas. Remarkably, the increased activity to HSF compared to LSF resembles activity patterns seen in healthy adults to grating stimuli (Boeschoten et al., 2005; Plant, 1983; Reed,

Marx & May, 1984; Vassilev, Mihaylova & Bonnet, 1983; Kenemans et al. 2000; Baas et al., 2002). Based on these findings, we suggested that the parvocellular system, which is tuned to high contrast HSF information, might be more developed in 3-4-year-olds with ASD compared to typically developing age-matched children. However, since we recorded activity from cortical neurons, which are not linked in a one-to-one manner with the parvo- and magnocellular system (Skottun & Skoyls, 2007), alternative explanations should also be considered. It is well possible that the enhanced neural processing of HSF gratings in children with ASD is due to other abnormalities in visual cortical areas (e.g. neuronal tuning to a higher range of SFs), or abnormalities in the macular part of the retina, which is also important for the processing of detailed information. Abnormalities in HSF processing in ASD have been reported before in older children (mean age: 10 years) by Boeschoten, Kemner, Kenemans and van Engeland (2007) in a source localization study. In this study, abnormal sources were found to underlie the ERP responses to HSF gratings in these children. Compared to controls, HSF gratings already activated secondary processing areas, whereas in controls, sources of neural responses to HSF gratings were located in primary visual areas.

As was discussed in the introduction of this thesis, the Enhanced Perceptual Function hypotheses of Mottron et al. (2006), assumes that in ASD there is overdevelopment of visual areas presumably leading to enhanced perceptual stimulation. Mottron et al. (2007) suggest that the atypical peripheral looking or lateral glances in ASD (looking from the corner of the eye) that occur in young children with ASD, might be seen as a strategy to avoid such perceptual overload, that might for example arise through enhanced processing of HSF. That is, the sensitivity of the visual system for HSF information is highest at the fovea and decreases when it is farther away from the fovea (towards the corner of the eye or periphery) (see for review Henriksson, Nurminen, Hyvärinen & Vanni, 2008). Therefore, peripheral looking might reduce HSF processing.

Differences in the role of SF in facial expression processing

Importantly, the study described in chapter 3 indicates that abnormalities in spatial frequency processing are not restricted to non-social (grating) stimuli in 3-4 year olds with ASD, but are also seen in early stages of facial expression processing in the same age group. Consistent with the finding of enhanced processing of HSF gratings, we found that in young children with ASD, early processing of facial expressions in visual brain areas is mainly based on HSF, whereas in controls the processing of emotion was primarily driven by LSF (global information). As described in chapter 3, this is in agreement with several suggestions that the rapid LSF 'quick and dirty' route for face processing, involving the amygdala, is dysfunctional in ASD (Laycock, Crewther & Crewther, 2007; John-

son; 2005; Deruelle et al., 2008). However, ERP data does not directly reflect subcortical activity. The rapid extraction of emotion based on LSF could also be driven by a rapid feedforward projection from other visual areas. Other techniques, well suited for recording activity from subcortical areas like fMRI, should shed more light on this issue.

In paragraph 6.1 we suggested that young children might still be more tuned to LSF than HSF for rapid emotion extraction due to immaturity of HSF processing. In light of this explanation, the presence of an effect of emotion in HSF on the P1 in 3-4 year-old children with ASD, in contrast to controls, might reflect that HSF processing is more mature in children with ASD, which would also be in agreement with the finding of a more 'adultlike' pattern of activity to HSF in the grating task. HSF sensitivity might be already present from birth in processing might be even enhanced from birth on in ASD due to abnormalities in the visual system (see for further suggestions paragraph 2 of this section).

It would be interesting to investigate whether an "HSF bias" for facial expression processing in ASD, continues to be present later on in life. Behavioral findings, showing that explicit emotion recognition and identity recognition is primarily driven by HSF in older children and adults with ASD, suggest that this is indeed the case (Deruelle et al., 2008; Curby, Schyns, Gosselin & Gauthier, 2003; Deruelle et al., 2004). In addition, a recent study indicated that the processing of gaze cues in older children is biased towards the use of HSF information (de Jong, van Engeland & Kemner, 2008).

Besides older children and adults, it would also be interesting to include infants to be able to explore how abnormalities in spatial frequency processing relate to the type of objects or features infants with autism preferentially attend to early in life. Enhanced processing of HSF, compared to LSF, in infancy might influence face orienting early in life. It has been suggested that there is an innate mechanism that is sensitive to the configuration of a face, which is responsible for face orienting in infancy (see for review Johnson, 2005). Because the configuration of a face is best captured in LSF information (see for review Goffaux & Rossion, 2006), an imbalance in the processing of SF early in life might influence face orienting by attracting attention to other types of stimuli, than faces.

6.4 Some controversial findings and methodological aspects on the role of SF in facial expression processing

Until now, only two ERP studies investigated the contribution of SF to the early processing of facial expressions in the visual brain in healthy adults (Holmes, Winston & Eimer, 2005; Pourtois et al., 2005). However, results of these studies are inconsistent with respect to each other, as well as the previous studies (see

chapter 4). In chapter 4, we concluded that the inconsistency in results of these studies might be related to differences in the types of stimuli as well as tasks that were used. Because of these controversial findings, we again investigated the role of SF in early facial expression processing in the visual brain, using stimuli that have been shown to elicit emotion processing during early processing stages, when using a passive task (Blau, Maurer, Tottenham & McCandliss, 2007). We analyzed two different ERP peaks, which index relatively early stages of facial expression processing in visual areas, the P1 and N170.

Additionally, an important problem in the investigation of SF processing was addressed. That is, LSF and HSF filtered stimuli differ not only at the level of the spatial scale of information they convey, but also in terms of luminance and contrast. This is related to the fact that the frequency power in natural stimuli is maximal at low SF and almost exponentially decays at higher SF (see for review Loftus & Harley, 2005). Therefore, finding an effect of emotion in LSF but not HSF might be simply due to the fact that HSF stimuli are less luminant and of lower contrast. Therefore, to exclude the possibility that SF differences in emotion processing would be caused by contrast and luminance differences between HSF and LSF, we compared emotion processing when luminance and contrast were or were not equated across LSF and HSF, *within* one study. Besides examination of the early stages of emotion processing, we also investigated whether the differential involvement of HSF and LSF in face processing and contrast/luminance differences are reflected in behavior, when subjects have to rapidly categorize fearful and neutral expressions.

Our findings indicate that facial expression processing is primarily based on LSF at the level of the N170. Importantly, this effect was not influenced by changes in contrast or luminance, confirming the role that LSF information plays in the early processing of emotion (Pourtois et al., 2005; Holmes, Green & Vuilleumier, 2005). At the earlier P1 peak, emotional processing was also primarily driven by LSF, but only in the condition where images were contrast-luminance equated, possibly because early visual ERP components are very sensitive to luminance and contrast alterations (Blau et al., 2007; Ellemberg, Hammarrenger, Lepore, Roy & Guillemot, 2001). Therefore, contrast and luminance differences across HSF and LSF trials might have obscured early cortical (P1) differences related to emotion expression processing of non-equalized face images. In the behavioral categorization task, we found an effect of facial expression in both HSF and LSF conditions, irrespective of contrast equalization. Participants decided more quickly that a face was fearful, compared to neutral, irrespective of SF content and contrast or luminance differences. However, reaction times reflect the outcome of information processing and, as suggested earlier, it is well possible that at later stages of facial expression processing, HSF information is also valuable for emotion extraction.

Our findings complement two fMRI studies that showed that LSF is associated with amygdala activity to fearful faces (Vuilleumier et al., 2003; Winston et al., 2003). On the basis of these findings, Vuilleumier et al. (2003) argued that LSF components might have rapid access to the amygdala, either through a direct subcortical tecto-pulvinar route which is preferentially tuned to LSF information, or through an initial feedforward sweep of inputs within the visual system. Such a mechanism would allow for a rapid enhancement of activation in visual areas in response to fearful stimuli. Here, we provide high-temporal resolution evidence that LSF input is processed fast and drives the early processing of facial expressions in visual areas. As also discussed in paragraph 6.1, it remains to be investigated whether the early LSF effects on the processing of fearful expressions, reflect modulatory effects of a subcortical route, including the amygdala, or result from a rapid feedforward projection within the visual system.

In the studies in chapter 2 and 3 HSF and LSF stimuli were not matched on contrast and luminance. That is, HSF stimuli were less luminant and contained less contrast compared to LSF stimuli. It is well possible that this contributed to the absence of emotion expression effects when faces were presented in HSF in 3-4 year-old typically developing children. However, all the more interesting are the findings in the 3-4 year-old children with ASD, whose visual system seems to rapidly extract emotion based on HSF cues, even when HSF stimuli are of lower contrast and luminance.

6.5 Self-monitoring and ACC functioning in ASD

In the experiment in chapter 5, another important aspect of ASD was studied, namely problems in self-monitoring. Whereas most studies in this thesis focus on early visual development, deficiencies in other areas like general executive functioning are seen in ASD, for example in self-monitoring which plays an important role in social interactions (Russell & Jarrold, 1998). Interestingly, the ACC, a structure which has been reported to function abnormally in ASD, has been suggested to play an important role in the development of self-monitoring from late childhood to adulthood (Davies, Segalowitz, & Gavin, 2004; Ladouceur, Dahl & Carter, 2007). The ERP study in chapter 5 was aimed at directly investigating whether ACC functioning is abnormal during self-monitoring in children with ASD (mean age: 10 years; range 7-14 years) using ERPs. A specific type of self-monitoring was studied, namely response monitoring, this is the monitoring of correct and incorrect responses. In addition, post-error slowing in reaction times was measured, which is thought to be indicative of adjustment of response strategies after an error has been made (e.g. Gehring & Fencsik, 2001; Bogte, Flamma, van der Meere & van Engeland, 2007).

Reduced brain activity in response to errors was found in the early as well as later stages of error processing in ASD, respectively reflecting error or conflict detection and conscious error evaluation. Furthermore, the behavioural data showed an additional lack of post-error slowing of reaction times in this group compared to control children. The reduced neural activity in response to errors in ASD, in combination with intact activity to correct responses, might suggest a specific insensitivity to detect situations in which the chance of making errors is enhanced. This might in turn lead to reduced error awareness or attention allocation to the erroneous event, in later stages of processing. This might eventually lead to a failure in change of strategy to deal with a situation, as becomes evident from the lack of post-error slowing in the ASD group. The present findings relate well to the repetitive and perseverative behavior that is sometimes seen in ASD (Bogte et al., 2007; Henderson et al., 2006).

Importantly, the sources underlying the neural responses during the earliest stage of error processing could be located in the ACC area in both controls as well as children with ASD, in accordance with previous studies in adults (Luu, Flaisch & Tucker, 2000; Hermann et al., 2004; van Veen & Carter, 2002). As is discussed more elaborately in chapter 5, in light of the developmental literature, the reduced activity in the ACC region in children with ASD may reflect immaturity or impaired functioning of the ACC and/or connected regions and/or related neurotransmitter systems. Deficiencies in ACC functioning have been found before in adults with ASD (Haznedar, Buchsbaum, Metzger, Solimando, Spiegel-Cohen & Hollander, 1997; Haznedar et al., 2000; Ohnishi et al., 2000). When reviewing the clinical literature (see chapter 5), the combination of reduced (ACC) activity during error processing as well as a lack of post-error slowing seems to be quite specific to ASD, although there might be overlap with ADHD. Additional research in ASD and ADHD needs to further investigate this suggestion.

How do the data of chapter 5 relate to abnormalities in visual processing in ASD? Self-monitoring can be considered as a higher order control or 'frontal lobe' function. Besides deficits in self-monitoring and ACC functioning, there are several recent studies that have reported reduced frontal lobe activity (see for review Mottron, Dawson, Soulières, Hubert & Burack, 2006) or reduced or abnormal connectivity between frontal areas and lower order areas in various tasks in ASD (see for a recent review Kleinhans et al., 2008). A recent model by Mottron et al. (2006) describes a link between relative strengths/abnormalities in visual functioning and deficiencies in higher order control in ASD. Mottron et al. (2006) suggest that low-level perceptual processing is abnormally enhanced relative to high-level cognitive processes, making automatic perceptual processes more difficult to control by top-down mechanisms and thus more likely to supersede or interfere with higher cognitive processes. According to Mottron et al. (2006), this would be reflected in a general "skewing" of brain activity towards

visuo-perceptual regions relative to higher order regions (frontal), which has indeed been found in several tasks in ASD including the Embedded figures task (Ring et al., 1999; Manjaly et al., 2007; Lee et al., 2007), Block design task (Bölte, Hubl, Dierks, Holtmann & Poustka, 2008) and visual-spatial covert attention shifting tasks (Belmonte & Yorgelun-Todd, 2003), but also word learning (Hazlett et al., 2004), N-back task and visuo motor tasks (Koshino, Carpenter, Minshew, Cherkassky, Keller & Just, 2005; Müller, Kleinhans, Kemmotsu, Pierce & Courchesne, 2003). In the study in chapter 5, we also found evidence for a decrease in frontal (error-related) activity. In a prior study, including the same subjects and the same task, enhanced activity in the visual areas was found in response to visual probes in ASD children in the interval in which the child had to respond and could possibly make an error (Hoeksma, Kemner, Verbaten & Van Engeland, 2005).

In contrast to the suggestion of Mottron et al. (2006), that an increased autonomy and enhanced processing in more downstream areas leads to deficiencies in higher order control in ASD, it is also well possible that due to abnormalities in development of the frontal areas and connections between frontal areas and lower order areas, there is an overdevelopment of lower order areas (e.g. visual areas), which causes relative strengths in visual processing. Based on the data presented in this thesis, it is impossible to distinguish between these explanations as they were not aimed at studying the development of abnormalities in visual processing in relation to the frontal areas. Future developmental studies should be aimed at further investigating this, by carefully monitoring the relationship between the development of lower and higher order processing in ASD.

6.6 Limitations

The studies described in this thesis contribute to a better understanding of the normal and abnormal development of rapid facial expression processing, yet some methodological considerations have to be made.

With respect to the studies that addressed the role of SF in rapid processing of facial expressions it is important to note that only one type of facial expression was used in the studies, namely fearful facial expressions (which were compared to neutral expressions). It thus is as yet unclear whether the findings of the role of SF in facial expression processing will generalize to other categories of facial (emotional) expressions.

In addition, we would like to emphasize that the studies described in this thesis were aimed at specifically investigating the role of HSF and LSF in facial emotional expression processing. We did not include SF bands in between, which might also play a role in the rapid processing of facial expressions and might show different developmental trajectories in its involvement in facial expression

processing. Furthermore, it must be noted that we studied the contribution of HSF and LSF to face processing separately. However, there are studies that have indicated that for some tasks, SF information is combined and processed in an interactive way (see for review Hess, 2005). With respect to face processing, it is for example well possible that the processing of LSF information facilitates the processing of HSF in that it serves as a kind of header to refine the face percept progressively, as has been suggested by Goffaux & Rossion (2006). In the present study we did not take this into account.

Also, although a considerable number of ASD children were included in the grating task, the group of children that took part in the task investigating the role of SF in facial expression processing, was much smaller. Future studies should be aimed at including larger groups. Moreover, we would like to emphasize that the results we found in young children with ASD, apply to the present age groups only, and should not be generalized to ASD in general. As seen in our developmental study, there are large developmental differences in SF processing in typical development.

6.7 Conclusions and implication for future research

Returning to the general research aims the following conclusion can be drawn from the data and implications can be made for future research:

An integration of the results from chapter 2 and 3 shows that there are developmental differences in the type of information that serves the early processing of emotional expressions in the visual brain. Possibly because, the ability to resolve HSF is not yet mature at the age of 3-4 years, relevant emotional cues cannot be rapidly resolved from HSF, and as a consequence the processing of emotion is based on LSF in the first stage of facial expression processing that was measured. At a later stage, emotion processing was driven by HSF. In older children (5-8 years), at which age the ability to resolve HSF is fully mature, emotional processing is primarily driven by HSF at both early and late processing stages. However, still the pattern that is seen in adults has not been reached at this age. That is, in adults facial expression processing, as reflected by both early and later ERP peask is primarily based on LSF (see chapter 5). We suggested that the shift to LSF towards adulthood might be related to an increase in face expertise across child development. On the other hand it might be related to developmental differences in the visual system and/or parts of the brain that are involved in the processing of emotion. Future studies should be aimed at further investigating when the processing of emotion starts to be primarily based on LSF and what the underlying mechanism behind this developmental effect is. A better understanding of the normal development might contribute to a better comprehension of

developmental disorders like autism, in which difficulties in facial expression processing as well as SF processing have been found.

The studies described in chapter 3 indicate that, compared to typically developing children young children with ASD show a basic abnormality in visual processing, more specifically enhanced processing of HSF, which is also reflected in the processing of emotional signals captured in faces. Abnormalities in SF processing have been reported before in older children and adults with ASD and have been related to the often reported detailed processing style in ASD. For the first time, we indicate that enhanced processing of HSF is already present early in life in ASD and that it influences face processing. The exact mechanism behind this is as yet unclear. Future studies (possibly in even younger age groups) should be aimed at further investigating this. In addition, it is important to examine how abnormalities in spatial frequency processing relate to the type of objects or features the autistic infant naturally attends to early in life and whether they are involved in reduced face orienting at that age. Furthermore, from the point of view of treatment of autistic children it is important to examine whether the enhanced processing of details in ASD might explain the visual over stimulation, which some adults with ASD report to suffer from during their lifetime (Faherty & Mesibov, 2000), and to consider how this might be prevented.

The study described in chapter 3 indicates that differences in luminance and contrast between HSF and LSF images, which are a consequence of the filtering procedure, do not explain the dominance of LSF in an early stage of emotion processing (reflected in N170). However, with respect to the initial stage of processing that was measured (at the P1), results are less clear. Future studies aimed at investigating the role of SF in face processing should take this into account.
In chapter 5 another aspect of ASD was addressed. Besides abnormalities in visual processing, people with ASD show deficits in areas of functioning that involve higher order processing, for example in self-monitoring a function that is important for social development. We indicated reduced involvement of the ACC region during self-monitoring, more specifically during the processing of erroneous responses, in school age children with ASD. In addition, an absence of change in behavioral strategies after the commission of an error was found. This relates well to the inflexible and sometimes repetitive behavior that is often seen in ASD.

The results of chapter 3 and 5, that show abnormaltities in low level visual processing as well as higher order processing in ASD, relate well to recent models which suggest that low-level perceptual processing is abnormally enhanced relative to high-level cognitive processes, making automatic perceptual processes more difficult to control by top-down mechanisms and thus more likely to supersede or interfere with higher cognitive processes. As a next step, future studies could be aimed at integrating the different abnormalities that have been found in ASD. For example, by investigating whether there is a direct relation between

enhanced low-level (visual) and diminished higher order processing in ASD. Taking such a perspective is also important when studying normal development (e.g. visual or emotional) to better understand how certain brain areas and their corresponding functions develop in relation to each other. Combining different research methods (e.g. EEG and fMRI) and the use of functional connectivity analyses open up new possibilities and may play an important role in this.

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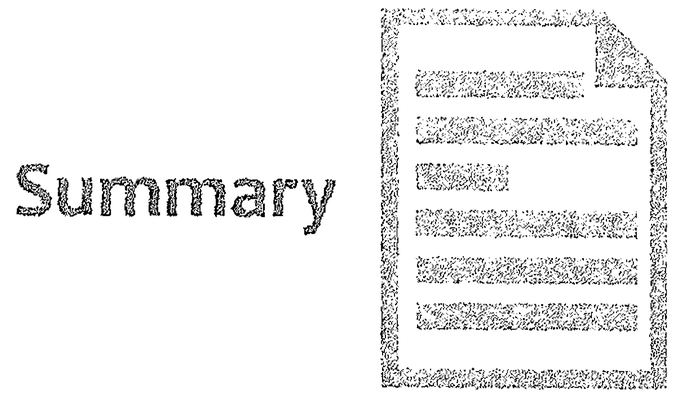

Summary

Chapter 6

Rapidly perceiving the emotional content of a face is an important skill for successful social behavior, since it helps to evaluate the states and intentions of others and to adapt future behavior. One of the ways in which the visual system captures environmental information, like facial expressions, is in terms of luminance variations (light-dark transitions) across space. High spatial frequencies (HSF) represent abrupt, small luminance changes, corresponding to sharp edges and fine perceptual detail. Low spatial frequencies (LSF), on the other hand, represent global changes in luminance, and provide information about the general shape, proportions and large contours of objects in our visual environment. Several studies in adults have indicated that LSF play an important role in the rapid processing of facial expressions. Some studies have proposed a rapid subcortical face processing pathway, which is preferentially tuned to LSF and modulates activity in visual areas to provide early signals of emotional expressions, for example threat.

This perceptual side of facial expression processing is often overlooked, and is hardly taken in consideration when studying the development of normal and abnormal processing of facial expressions. The experiments described in this thesis, among others, address whether there are developmental differences in the type of spatial frequency information that is important for facial expression processing across childhood. In addition, the experiments examine whether abnormalities in spatial frequency processing are present in young children with Autism Spectrum Disorder (ASD) and whether this is related to abnormal facial expression processing in this group. It is important to look at this since facial expressions form an important basis for communicative and social development early in life when language is relatively immature.

Chapter 1 of this thesis provides an introduction to the main theoretical and methodological aspects of SF and facial expression processing. Thereafter, the experimental chapters follow which investigate a) whether there are developmental differences in the type of spatial frequency information, HSF and/or LSF, that is important for facial expression processing in typically developing children (3-8 years) (chapter 2) b) whether abnormalities in SF processing are present in young children with Autism Spectrum Disorder (ASD) and whether they contribute to abnormalities in facial expressions processing (chapter 3) c) some issues on the role of SF in facial expression processing in adults, especially the effect of luminance/contrast equalization in SF contributions to facial expression processing (chapter 4) d) another aspect of ASD, i.e. problems in self monitoring in school age children with ASD (chapter 5). To address these questions Event Related brain Potentials (ERPs) were used, a technique that it is well suited to study early influences of for example emotion and SF on processing in the (visual) brain. In chapter 6, the findings of the studies in the different chapters are linked and discussed in light of the background literature.

An integration of the results from chapter 2 and 3 shows that there are developmental differences in the type of information that serves the early processing of emotional expressions in the visual brain. Possibly because, the ability to resolve HSF is not yet mature at the age of 3-4 years, relevant emotional cues cannot be rapidly resolved from HSF, and as a consequence the processing of emotion is based on LSF in the first stage of facial expression processing that was measured. At a later processing stage, emotion processing is driven by HSF in 3-4 year-olds. In older children (5-8 years), at which age the ability to resolve HSF information is fully mature, emotional processing was primarily driven by HSF at both early and late processing stages. However, still the pattern that is seen in adults has not been reached at this age. That is, in adults emotional expression processing, as reflected by both early and later ERP peask is primarily based on LSF (see chapter 5). We suggested that the shift to LSF with age might be related to an increase in face expertise across child development. On the other hand it might be related to developmental differences in the visual system and/or parts of the brain that are involved in the processing of emotion. Future studies should be aimed at further investigating when the processing of emotion starts to be primarily based on LSF and what the underlying mechanism behind this developmental effect is. A better understanding of the normal development might contribute to a better comprehension of developmental disorders like autism, in which difficulties in facial expression processing as well as SF processing have been found.

The studies described in chapter 3 indicate that, compared to typically developing children, young children with ASD (3-4 years) show a basic abnormality in visual processing, more specifically enhanced processing of HSF, which is also reflected in the processing of emotional signals captured in faces. Abnormalities in SF processing have been reported before in older children and adults with ASD and have been related to the often reported detailed processing style in ASD. For the first time, we indicate that enhanced processing of HSF is already present early in life in ASD and that it influences face processing. The exact mechanism behind this is as yet unclear but could be related to several neural mechanisms, such as a more developed parvocellular system, abnormalities in visual cortical areas (e.g. neuronal tuning to a higher range of SFs), or abnormalities at the retinal level. Future studies (possibly in even younger age groups) should be aimed at further investigating the potential involvement of these different brain mechanisms. Furthermore, future studies should investigate whether the enhanced processing of HSF influences the type of visual objects the child with autism naturally attends to and whether it is responsible to the decreased face orienting in ASD.

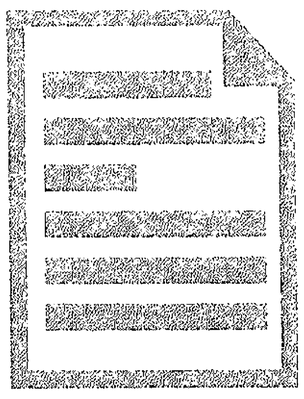
The study described in chapter 4 clearly shows that differences in luminance and contrast between HSF and LSF images, which are a consequence of the filtering procedure, do not explain the dominance of LSF in an early stage of emo-

tion processing in the visual brain (reflected in N170) in adults. However, with respect to the initial stage of processing that was measured (at the P1), results are less clear. Future studies aimed at investigating the role of SF in face processing should take this into account.

In chapter 5, another aspect of ASD was addressed. Besides abnormalities in visual processing, people with ASD show deficits in areas of functioning that involve higher order processing, for example in self-monitoring, a function that is important for social development. We indicated reduced involvement of the ACC region during self-monitoring, more specifically during the processing of erroneous responses, in school age children with ASD. In addition, an absence of change in behavioral strategies after the commission of an error was found. This relates well to the inflexible and sometimes repetitive behavior that is often seen in ASD.

The results of the studies on low level visual processing (chapter 3) as well as higher order processing (chapter 5) in ASD relate well to recent models which suggest that low-level perceptual processing is abnormally enhanced in ASD relative to high-level cognitive processes, making automatic perceptual processes more difficult to control by top-down mechanisms and thus more likely to supersede or interfere with higher cognitive processes. As a next step, future studies could be aimed at investigating integrating the different abnormalities that have been found in ASD For example, by investigating whether there is a direct relation between enhanced low-level (visual) and diminished higher order processing in ASD. Taking such a perspective is also important when studying normal development (e.g. visual or emotional) to better understand how certain brain areas and their corresponding functions develop in relation to each other. Combining different research methods (e.g. EEG and fMRI) and the use of functional connectivity analyses open up new possibilities and may play an important role in this.

Samenvatting



Samenvatting

Het snel waarnemen van gezichtsuitdrukkingen is belangrijk voor succesvolle sociale interacties. Een gezicht vertelt iets over de toestand waarin een ander verkeert en de intenties die een persoon heeft. Op basis daarvan kunnen toekomstige interacties en handelingen worden afgestemd.

Informatie, die via onze ogen het visueel systeem binnenkomt, is erg complex. Een van de manieren waarop het visuele systeem binnenkomende informatie uit de omgeving (zoals gezichtsuitdrukkingen) verwerkt, is op basis van veranderingen in luminantie; overgangen tussen licht en donker. Laag spatiële frequenties (LSF) representeren grote overgangen tussen licht en donker en verstrekken informatie over de globale vorm, proporties en contouren van objecten in de omgeving. Hoog spatiële frequenties (HSF) daarentegen representeren abrupte, kleine luminantie veranderingen, ofwel fijne details uit de visuele omgeving. Verschillende studies hebben aangetoond dat LSF informatie (globale informatie, zoals de contouren van een gezicht) van belang is voor de snelle verwerking van gezichtsuitdrukkingen. Sommige studies veronderstellen dat er een snelle subcorticale route is in het brein, die speciaal is afgestemd op LSF informatie en die zorgt voor een snelle modulatie van corticale activiteit zodat signalen van bijvoorbeeld dreiging snel kunnen worden afgegeven.

Het is opmerkelijk dat vaak voorbij wordt gegaan aan het perceptuele aspect van de verwerking van gezichtsuitdrukkingen. Dit aspect wordt nauwelijks in acht genomen in studies naar de normale en abnormale ontwikkeling van de verwerking van gezichtsuitdrukkingen. De experimenten in dit proefschrift bestuderen onder andere of voor kinderen, het type visuele informatie (LSF en/of HSF) dat van belang is voor de verwerking van gezichtsuitdrukkingen, verandert tijdens de ontwikkeling in de kindertijd. Daarnaast is het doel van de experimenten om te onderzoeken of jonge kinderen met een Autisme Spectrum Stoornis (ASS) afwijkingen vertonen in de verwerking van HSF en/of LSF informatie. Ook wordt bekeken of eventuele afwijkingen in SF verwerking zich weerspiegelen in de verwerking van emotionele gezichtsuitdrukkingen in ASS. Het is belangrijk dit laatste te bestuderen omdat gezichtsuitdrukkingen een belangrijke basis vormen voor communicatieve en sociale ontwikkeling, waarin kinderen met ASS achterblijven bij leeftijdsgenoten.

Hoofdstuk 1 vormt een introductie tot de belangrijkste theoretische en methodologische aspecten van SF en de verwerking van gezichtsuitdrukkingen. Na hoofdstuk 1 volgen de experimentele hoofdstukken die studies beschrijven die:

a) onderzoeken of voor normaal ontwikkelende kinderen (3-8 jaar) het type visuele informatie (HSF en/of LSF) dat van belang is voor de verwerking van gezichtsuitdrukkingen verandert tijdens de ontwikkeling (hoofdstuk 2).
b) onderzoeken of kinderen met ASS, afwijkingen vertonen in de verwerking van HSF en/of LSF informatie en of eventuele afwijkingen zich weerspiegelen in de verwerking van emotionele gezichtsuitdrukkingen (hoofdstuk 3).

c) in een groep volwassenen, een aantal technische aspecten belichten, die gerelateerd zijn aan de rol van SF in de verwerking van emotionele gezichtsuitdrukkingen. Daarbij gaat het specifiek om de invloed van luminantie- en contrastvereffening op de bijdrage van SF aan de verwerking van gezichtsuitdrukkingen (hoofdstuk 4).
d) een ander aspect van de ASD problematiek belichten, namelijk afwijkingen in het letten op en evalueren van eigen acties (ook wel zelf-monitoring genoemd), in een groep schoolkinderen met ASS.

Tot slot worden in hoofdstuk 6, de bevindingen van de studies uit de verschillende hoofdstukken besproken in relatie tot de achtergrondliteratuur.

Het combineren van de resultaten van hoofdstuk 2 en 3 geeft aan dat er ontwikkelingsverschillen zijn in het type informatie dat van belang is voor de verwerking van gezichtsuitdrukkingen tijdens de eerste stadia van de visuele verwerking in het brein. In tegenstelling tot de oudere kinderen werd door de jongste groep kinderen (3-4 jaar) in het eerste stadium van de visuele verwerking emotionele informatie niet verwerkt op basis van HSF, mogelijk omdat kinderen op deze leeftijd HSF nog niet voldoende kunnen waarnemen. Verwerking van emotie door 3-4 jarigen vond in dit stadium plaats op basis van LSF. De waarneming van LSF is al wel voldoende ontwikkeld op deze leeftijd. Contrasterend met het eerste stadium werden, in een later stadium van de visuele verwerking, emotionele expressies wel verwerkt op basis van HSF door de 3-4 jarigen. In de groep oudere kinderen (5-8 jaar), vond de verwerking van emotie plaats op basis van HSF in zowel de vroege als late stadia van visuele verwerking. Het volwassen patroon, verwerken van gezichtsuitdrukkingen op basis van LSF in zowel vroege als latere stadia (zie hoofdstuk 5), lijkt nog niet bereikt te zijn in de leeftijdsgroepen die onderzocht zijn in de huidige studie. In hoofdstuk 6 wordt gesteld dat een verschuiving naar LSF informatie met leeftijd mogelijk gerelateerd kan zijn aan toenemende expertise met gezichtsuitdrukkingen. Aan de andere kant is het ook mogelijk dat een dergelijke verschuiving gerelateerd is aan de ontwikkeling van het visuele en/of andere delen van het brein, die betrokken zijn bij de verwerking van emotie. Vervolgstudies moeten hier verder inzicht in geven.

De studies uit hoofdstuk 3 laten voor het eerst een basale afwijking in de verwerking van visuele informatie zien in kinderen met ASS (3-4 jaar). Dat wil zeggen, uit de resultaten blijkt dat kinderen met ASS HSF informatie versterkt verwerken en dit is ook zichtbaar in de verwerking van gezichtsuitdrukkingen. Afwijkingen in SF verwerking zijn eerder waargenomen bij oudere kinderen en volwassenen met ASS en worden gerelateerd aan de detaillistische informatieverwerkingsstijl die vaak wordt gevonden bij mensen met ASS. In de studies in hoofdstuk 3 wordt voor het eerst aangetoond, dat het versterkt verwerken van HSF al op jonge leeftijd aanwezig is in ASS en dat dit ook terugkeert in de verwerking van gezichten. Op basis van de huidige studies is het niet mogelijk het

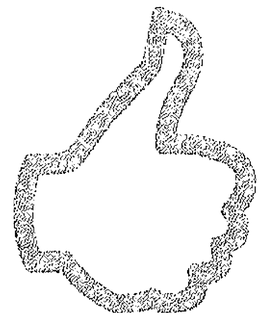
mechanisme hierachter te duiden, het zou gerelateerd kunnen zijn aan een beter ontwikkeld parvocellulair systeem, maar ook aan afwijkingen in de visuele cortex (bijvoorbeeld neuronale tuning tot een hogere range SFs), of abnormaliteiten op het niveau van de retina. Vervolgstudies (mogelijk in jongere leeftijdsgroepen) moeten de betrokkenheid van deze mechanismen verder uitwijzen. Daarnaast dienen toekomstige studies te onderzoeken of de gevonden afwijking in SF verwerking het kijkgedrag van kinderen met ASS beïnvloedt en of het verantwoordelijk is voor het gereduceerd kijken naar gezichten waardoor ASS gekenmerkt wordt.

Hoofdstuk 4 geeft aan dat in volwassenen de dominantie van LSF in een vroeg stadium van de visuele verwerking (N170) van gezichtsuitdrukkingen niet verklaard kan worden door verschillen in luminantie en contrast tussen HSF en LSF afbeeldingen. Verschillen in contrast en luminatie lijken wel een rol te spelen in een eerder stadium van dat gemeten werd (P1). Toekomstige studies die gericht zijn op het onderzoeken van de rol van SF in de verwerking van gezichtsinformatie dienen hier rekening mee te houden.

In hoofdstuk 5, wordt een ander aspect van de ASS problematiek belicht. Naast afwijkingen in de verwerking van visuele informatie vertonen mensen met ASS deficiënties in meer complexe, hoge orde processen, bijvoorbeeld in zelfmonitoring, een functie die belangrijk is voor sociale ontwikkeling. De resultaten van de studie uit hoofdstuk 5 tonen een reductie in activiteit in de regio van de Anterior Cingulate Cortex (ACC) in schoolkinderen met ASS tijdens zelfmonitoring. Ook werd gevonden dat kinderen met ASS gedrag niet aanpassen na het maken van een fout, hetgeen ook duidt op verminderde zelf-monitoring. De resultaten van dit hoofdstuk passen bij het inflexibele en soms repetitieve gedrag dat voorkomt in ASS.

Zowel de resultaten van de studies naar lage orde visuele verwerking (hoofdstuk 3) als studies naar hoge orde processen (hoofdstuk 5) passen bij recente modellen die veronderstellen dat lagere orde visuele processen versterkt zijn in ASS ten opzichte van hogere orde cognitieve processen. Verondersteld wordt dat hierdoor automatische visuele processen in ASS moeilijker gecontroleerd kunnen worden door middel van top-down, hoge orde controle processen. Automatische visuele processen kunnen hierdoor interfereren met hoge orde processen. Vervolgonderzoek dient zich te richten op integratie van de verschillende afwijkingen die gevonden zijn in ASS. Bijvoorbeeld door te onderzoeken of er een directe relatie is tussen versterkte lage orde (visuele) en verminderde hoge orde verwerking in ASS. Een dergelijk perspectief is ook belangrijk voor studies naar de normale ontwikkeling (bijvoorbeeld op visueel of emotioneel gebied), met het doel een beter inzicht te vergaren over hoe bepaalde hersengebieden en bijbehorende functies zich ontwikkelen in relatie tot elkaar. Het combineren van verschillende onderzoeksmethoden (bijvoorbeeld EEG en fMRI) en het gebruik van functionele connectiviteits-analyses creëert nieuwe mogelijkheden en zou hier een belangrijke rol in kunnen spelen.

Dankwoord



Dankwoord

Wetenschap bedrijven doe je niet alleen. De studies beschreven in dit proefschrift zijn tot stand gekomen door samenwerking met veel verschillende mensen, die ik hier wil bedanken. Ook wil ik degenen bedanken die indirect hebben bijgedragen aan de totstandkoming van dit proefschrift.

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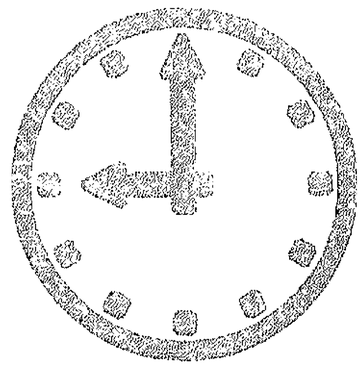
Curriculum Vitae



Curriculum Vitae

Petra Vlamings was born on September 24th 1981 in Boxtel, The Netherlands. She attended the Jacob-Roeland Lyceum, where she obtained her Gymnasium diploma in 1999. She started to study psychology at Maastricht University in 1999, where she became a teaching assistant in 2000. In this period she specialized in developmental psychology. Her master thesis described several comparative behavioral studies on executive functioning in the four species of Great Ape which she performed during her research internship (2002-2003) at the Max Planck Institute Leipzig (Germany), department of developmental and comparative psychology under supervision of Dr. Josep Call. There, she was also employed as a research assistant. Thereafter she performed a clinical traineeship at the Michaëlsschool (Rec 4) in Boxtel and worked as a research assistant under supervision of Dr. Lisa Jonkman at Maastricht University, department of Cognitive Neuroscience, section Developmental Cognitive Neuroscience. In 2004, she graduated with a specialization in developmental psychology (cum laude). In the same year she was employed as a Ph.D student at the department of Cognitive Neuroscience, section Developmental Cognitive Neuroscience, at Maastricht University. During this period she conducted the studies described in this thesis in collaboration with Karakter, Academical Center for Child and Adolescent Psychiatry in Nijmegen and the department of Child and Adolescent Psychiatry in Utrecht under supervision of Prof. Dr. Chantal Kemner and Dr. Lisa Jonkman.

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